HILBING'S MODERN MATERIA MEDICA

MODERN MATERIA MEDICA

FOR

Pharmacists, Medical Men, and Students,

BY

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INTRODUCTION TO THIRD EDITION.

During a period of twelve months no branch of science in this age stands still. New experiments are constantly being devised and carried out, old ones are repeated; innumerable new facts are brought to light and relationships hitherto unsuspected or only guessed at are established between those already ascertained; everywhere the spirit of investigation, the spirit of inquiry is at work.

Perhaps nowhere is this restless progressive tendency more conspicuous than in pharmacology, and especially in that of the synthetical class of remedies which forms the principal subject of this work. It is true that the study of all the remedies has not been advanced to the same degree and that a few seem to have been even entirely neglected, but with these rare exceptions, the literature—chemical in a number of cases, pharmacological in a great many—of the substances treated in the preceding edition has developed and increased to a marked extent.

These additions not only constitute fresh material to be included in a revised edition of Modern Materia Medica, but in a large number of cases have an effect upon the balance of opinion which has been expressed upon the value of certain of the substances treated.

For this reason it has been found necessary to entirely rewrite those parts which summarise the therapeutical uses of the compounds, while in a considerable proportion of cases the same has been made necessary in the other divisions of the monographs by the publication of recent researches on the chemistry of the synthetical remedies.

This revision and extension of the subjects of the preceding edition and the inclusion of a number of entirely new additions to the class of substances treated have made it necessary to add about forty pages to—that is to increase by half as much again—the first part of the book.

Some of the new-comers have been considered to be of sufficient importance to require description in separate monographs, but a greater number has been added as "Derivatives and Allied compounds" to the chapters which appeared in the previous edition.

Even in the few weeks that have elapsed since these pages were closed for press papers have appeared on new substances which are being brought under the notice of medical men. Diaphtherin (oxychinaseptol) (OH. $C_9H_6N)_2$ (OH) (SO_3H) C_6H_4, and Asaprol (calcium–*β*–naphtol–*α*–monosulphonate) (OH. C_{10} H_6 $SO_3)_2$ Ca, 3 Aq., are antiseptics comparatively non-poisonous and soluble in water; the former is a powder which in 0.1 per cent. solution kills the cholera bacillus in 10 minutes, while the latter occurs in acicular crystals and in 5 per cent. solution prevents the growth of the most resistant bacilli.

The purpose and scope of the Appendix are sufficiently explained in the introductory words which immediately precede it. It has been very largely increased in bulk and includes a class of compounds (vegetable in origin) which, with a few exceptions, were not given a place in the second edition.

Special care has been taken with the terminology adopted in order to make it accord, so far as possible, with the rules which have been laid down by the best authorities for the guidance of English writers on chemical subjects.

London: May, 1892.

INTRODUCTION TO SECOND EDITION.

Synthetical remedies have become one of the distinctive features of our time. The zeal and untiring energy of the old alchemists in their search for the philosopher's stone and the elixir of life are reproduced to-day in the eager quest of their scientific descendants for artificial alkaloids.

Since the time when the modern chemist first became fired with the ambition to win fame and wealth at one stroke by the synthesis of quinine, the number of remedies turned out yearly from the chemical laboratory has gone on steadily increasing, and if the original aim of the work is still unaccomplished—as the process of M. M. Grimmaux and Arnaud is but a partial solution of the problem—yet among the very considerable number of compounds produced, some have been found capable of replacing the natural alkaloid in many cases, while in others they seem to be even superior to it in therapeutical activity, reliability or safety.

Not a few of the medical agents, thus, as it were, created, have won the favour of the medical profession sufficiently to secure them a place in the chief European Pharmacopœias. But there is a much larger number, the members of which are still on trial—passing through their period of probation—and of these, of course, there is no official recognition. Nevertheless their importance is, in some instances, not at all inferior to that of the pharmacopœial compounds, and hence they are more or less generally used by the medical man, and cannot be ignored by the pharmacist who desires to keep abreast of the times.

Naturally, however, the literature of substances produced at different times by various manufacturers and examined by pharmacologists and chemists in all parts of Europe and of the civilized world is widely scattered, and not easy to come at. For this and other more or less potent reasons it has become exceedingly difficult, if not impossible, for the busy medical man or pharmacist to maintain his acquaintance with the properties and uses of therapeutical novelties continually being brought under his notice in the scientific press of the country.

To be *au courant* with the growth of synthetical materia medica, however desirable, is, however, not all that the followers of medicine and pharmacy require. Information of this kind, if it is to be of practical service, must be in such a form as to be available for ready and more or less frequent reference.

It is the aim of the following pages to supply the want generally felt in this country of full and comprehensive details as to the constitution, methods of preparation, tests and medicinal application of new remedies. The requirements not only of the pharmacist, but also of the therapeutist and general practitioner, have been kept in mind; while further, the work is designed to rank as a text book for purposes of study. It would, perhaps, be well to add that in dealing with "medical uses" of each compound, it has been a constant endeavour to indicate its therapeutical importance, where possible, rather by a careful balancing of the whole literature of the subject than by a detailed quotation of individual experiences and quotations.

Every monograph has been carefully revised and extended, where necessary, in order to make the volume representative of the progress of synthetical remedies down to the date of issue. It is believed, that the practical value of the work to all classes of readers will be enhanced by the appendix, the various tables, and not less by the index, with which equal care has been taken.

London: June, 1891.

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MODERN MATERIA MEDICA.

ACETANILIDE.

Synonyms : Antifebrine ; Phenylacetamide.

$C_6H_5NH.CH_3CO.$

One of the most simple synthetical compounds of the "new remedy" era. Is now official in the British Pharmacopœia under the name "Acetanilidum."

Preparation.—By the prolonged interaction of pure aniline (boiling point 184° to 185° C.) and glacial acetic acid at a high temperature. Fractional distillation—collecting what passes over at 295° C.—and recrystallization from boiling water. The reaction may be thus represented :—

$$\underset{\text{Aniline}}{C_6H_5NH_2} + \underset{\text{Acetic acid}}{CH_3COOH} = \underset{\text{Acetanilide}}{C_6H_5NH.CH_3CO} + H_2O.$$

It should be observed that simple as this process appears on paper, it is practically very difficult to obtain a pure product even with special plant and large experience.

Physical and Chemical Properties.—When pure, acetanilide forms lustrous rhombic tables without color or odor, but with a peculiar greasy feel and a slight burning taste. It requires nearly 200 parts of water at 15° C. for solution, but only 18 of the same solvent at 100° C. (forming neutral solutions); soluble in alcohol (1 : 3½), readily in ether and in chloroform. According to the B. P. Addendum the crystals should melt at 112.8° C. (235° F.). When melted it forms a clear, colorless liquid, and distils unchanged at 295° C. By Ritsert the melting point of pure acetanilide is said to be 114° C., but the question is still an open one. By continued contact with hydrochloric acid or potash at high temperatures it splits up into its components.

Acetanilide is identified in the additions to the B. P. 1885 by the development of the odor of phenyl-isonitrile when heated with solution of potash and a few drops of chloroform. Other characteristic reactions are the formation of the yellow-

coloring substance with a beautiful moss-green fluorescence (flavaniline, $C_{16}H_{14}N_2$) when heated for some time with an equal weight of zinc chloride. Six grains boiled for a few minutes with 1 fl. drm. of hydrochloric acid form a clear solution, which, on the addition of 3 fl. drms. of water and 4 drops of carbolic acid previously dissolved in ½ fl. drm. of solution of chlorinated lime, assumes a turbid, dirty-red color, and, on the further addition of excess of ammonia, an indigo-blue (indophenol).

Free acetic acid is detected by the litmus reaction, acetone by ferric chloride, which must not affect the *cool*, aqueous solution, and aniline by solution of 15 grains in 1 fl. oz. of hot water (the solution is turbid if aniline be present, and smells of the latter). General impurities are detected by determination of the melting point and ignition on platinum foil (no residue should be left)

Ritsert states that a boiling solution of 15 grains in 1 fl. oz. of water is colored rose-red by one drop of a 0.1 per cent. aqueous solution of potassium permanganate, and that this color persists for at least five minutes.

Medicinal Uses.—Under the copy-righted name "antifebrine," acetanilide was introduced into medicine as an antipyretic in 1887. Its use in combatting the febrile temperature of acute rheumatism emphasized its analgesic virtues, and its principle employment has been in the treatment of neuralgias and rheumatism. As an antipyretic in phthisis, and other pulmonary affections, in typhus and fevers generally it has been largely replaced by remedies of more recent date, but it has been recommended within the last few months in the treatment of acute bronchitis (4 grains every two hours); the attacks were often arrested within 24 hours (Gruen). It has been credited with valuable properties in improving weak and irregular pains in labor.

There is considerable literature relative to the serious by- and after-effects which sometimes accompany or follow the remedial action of acetanilide. Though it is not improbable that these unpleasant experiences may have been in some cases due to impurity of the specimen used, yet it does appear that its employment requires watchful care.

The substance is not to be recommended for external application as an antiseptic.

The powerful physiological effects of acetanilide make it necessary to keep a watch upon its possible admixture, fraudulently or accidentally, with other synthetical antipyretics of which considerably larger doses are given.

The average dose of acetanilide is between 3 and 8 grains in powder, or wafers, capsules, etc. In certain conditions, *e. g.* in typhus, it is recommended to begin with quite small doses (1½ grains).

A purely pharmaceutical use of acetanilide has recently been suggested; its addition in small proportion to aqueous hypodermic solutions is said to preserve them from decomposition better than any other agent hitherto employed for the same purpose (Keenan).

DERIVATIVES AND ALLIED COMPOUNDS.

Mono- or *Para-Brom-Acetanilide*, also termed *Asepsine* and *Antisepsine*, was put forward some time after acetanilide had secured a footing in materia medica, as an anodyne, analgesic and antiseptic. Its literature is very scanty.

Salicylbromanilide, *Salbromalide*, and *Antinervine*, are the names under which a substance was brought under the notice of medical men early in 1890, and described as a combination of bromacetanilide and salicylanilide. According to an exhaustive examination by Ritsert, antinervine is a mixture of ammonium bromide, salicylic acid and acetanilide (1 : 1 : 2) and, therefore, cannot be administered with safety in quantities which contain more than the average dose of acetanilide.

Antikamnia. This name was given by an American firm to a preparation introduced as a substitute for morphine, and as an antipyretic and analgesic. It was manufactured as a fine white powder, which gave evidence of its non-homogeneity when examined under the microscope. Several analyses of "antikamnia" were published which all agreed in finding the chief constituents to be acetanilide with bicarbonate of soda. The proportions of these components seem from the analyses to have varied, and some observers detected caffeine, tartaric acid and other additions.

Phenolid was brought out as a competitor of "antikamnia." According to an analysis, published in America, it is a mixture of acetanilide and salicylate of soda, in the respective proportions of 58 : 43. A similar preparation has still more recently appeared from the New World, as

Exodyne (ἐξ and ὀδύνη, pain), a white powder, in which the microscope plainly reveals bodies of different crystalline form. Its average composition proved (Goldmann) to be acetanilide (90 per cent.), sodium salicylate (5 per cent.), and sodium bicarbonate (5 per cent.).

AMYLENE HYDRATE.

Synonyms: Dimethylethylcarbinol; Tertiary Amyl Alcohol.

$(CH_3)_2C_2H_5COH$.

One of the eight possible alcohols, with the general formula $C_5H_{12}O$. First prepared by Wurtz, and identified later by Flavytzky and Osipoff.

Preparation. — By the action of sulphuric acid upon amylene at a low temperature, separation of the amylenesulphuric acid, dilution with ice-cold water, filtration, neutralisation (with chalk or soda) and distillation. The distillate is freed from water by potash and fractionated, the fraction which passes over between 100° and 103.5° C. being collected.

Physical and Chemical Properties.—Amylene hydrate is a limpid, colorless, hygroscopic liquid, with a peculiar penetrating ethereal odor, which reminds of camphor and peppermint. Its specific gravity is 0.81, and when pure it boils at 102.5° C. In a mixture of salt and ice it solidifies at −12.5° C. to long acicular crystals, which melt at −12° C. Amylene hydrate dissolves in 8 parts of water at 15° C., the solution becoming turbid when warmed. It is miscible in all proportions with alcohol, ether and chloroform.

By oxidation with chromic acid it splits up into acetic acid and acetone.

Amylene hydrate is tested by determination of the physical factors. The liquid must not affect blue litmus (sulphuric acid) nor decolorize weak potassium permanganate solution

within 15 minutes (ethyl or amyl alcohol). 15 minims dissolved in ½ fluid ounce of water, to which are added 10 drops of argentic nitrate solution and 1 drop of ammonia, should not give a mirror or precipitate metallic silver when warmed (aldehyde). As already stated the liquid is hygroscopic, and therefore control must be kept upon the presence of water by the boiling point (which it lowers); by agitation of 2 fl. drachms with 10 grains of exsiccated cupric sulphate no powerful blue color should be produced.

Medicinal Uses.—This tertiary amyl alcohol was first recommended by Professor von Mering, who regarded it as specially useful in cases of nervous sleeplessness, as it did not manifest any action on the respiratory or circulatory systems. This lead was followed by other medical men (Avellis, Gürtler, Mayer, Rosenbach, Wildermuth), who ascribed anodyne as well as hypnotic properties to it. The adult dose adopted was 45 to 60 minims.

Two to five tablespoonful doses of a 10 per cent. aqueous solution have been effective in reducing the number of attacks in most forms of epilepsy (Naecke). When the patients have been previously taking bromide it would appear that considerable care is required, as in a number of cases of this kind the number of attacks increased and there was great restlessness. In a case which had resisted the action of all other remedies, amylene hydrate was also without effect (Drews).

In therapeutical activity amylene hydrate seems to be inferior to chloral, and it is not well borne when given for prolonged periods. It has proved successful in doses of 3 or 4 minims in the whooping cough of children.

Amylene hydrate is preferably given in solution (at least 8 parts of water being required), either aqueous or vinous, with raspberry syrup.

ANTHRAROBIN.

Synonym: Desoxyalizarin.

$$C_6H_4 \begin{Bmatrix} C(OH) \\ CH \end{Bmatrix} C_6H_2(OH)_2.$$

A phenol derivative, allied to chrysophanic acid, and described as a leuco-substance.

Preparation.—By the reduction of commercial alizarin in warm ammoniacal solution with zinc dust, and filtration of the resultant solution into water acidulated with excess of hydrochloric acid. The precipitate is washed by decantation until free from acid, collected on clay plates, and dried at 100° C.

Physical and Chemical Properties.—Commercial anthrarobin is a yellowish white powder, practically insoluble in water and dilute acids. Being a phenol derivative, it dissolves readily in the cold in dilute aqueous solutions of the alkalies and alkaline earths, these solutions being brownish-yellow, and greedily absorbing oxygen (by which alizarin is re-formed). Anthrarobin is difficultly soluble in chloroform and benzene, but readily in 5 parts of alcohol; also soluble in glycerine.

Twenty-four grains should dissolve in ½ fl. oz. of soda solution to a clear solution, which assumes a violet color if air is passed through it (1 grain absorbs 120 to 130 grain measures of oxygen). Should not leave more than 1 to 2 per cent. of residue when burned on platinum foil.

Medicinal Uses.—As a substitute for chrysarobin in skin diseases (Behrend), especially psoriasis. On the one hand its non-staining and unirritating properties have been commended (Liebermann and Pick), but on the other it has been characterized as practically worthless (Rosenthal and Köbner). No fresh reports have appeared upon its use for some time, and it seems to have been forgotten.

ANTIPYRINE.

Synonyms: Dimethylphenylpyrazolon; Dehydrodimethylphenylpyrazine; Phenazone; Methozine; Analgesine.

$$C_6H_5N \begin{cases} CO.CH \\ NCH_3.CCH_3 \end{cases}$$

A synthetical base which forms salts analogous to those of ammonia.

Preparation.—According to Knorr's patent by the interaction of phenylhydrazine and acetylacetic acid, whereby phenylhydrazine acetylacetate is formed. By the action of

heat this splits up into ethyl alcohol and phenylmethylpyrazolon, and the methylation of the latter in the presence of methyl iodide completes the process, antipyrine-hydriodide being actually formed.

By another method, recently patented, it is made by the condensation of a halogen butyrate and phenylhydrazine; the methylphenylpyrazine resulting is converted by a weak oxidizing agent into dehydromethylphenylpyrazine, and this by methylation yields dehydrodimethylphenylpyrazine.

It is interesting that according to recent researches (Michaelis and Lederer) the product of this second method is isomeric but not identical with antipyrine; the methyl groups in the two compounds are differently related to each other, the second being represented thus:—$C_6H_5N \begin{cases} CCH_3.CH \\ NCH_3.CO. \end{cases}$ The properties and action of the isomers are however quite similar, save in the particulars that isoantipyrine salicylate is difficultly crystallisable, and other salts of the two isomers exhibit differences in their physical properties.

Physical and Chemical Properties.—Antipyrine occurs in odorless and colorless scaly crystals, with a somewhat bitter taste. The melting point of the pure compound is 113° C. (B. P. Add. 110° C.); it is readily soluble in water, rectified spirit and chloroform, but less soluble in ether (about 1 in 50). Ignited with free access of air, it burns away without residue (absence of inorganic contamination).

The absence of free acid is insured by requiring the aqueous solution to react neutral to test-paper, and of metals by providing that the passage of sulphuretted hydrogen shall produce no effect. By nitrous acid the solution is turned a green color; this is one of the tests for identity adopted by the B. P. Add. Another given by the same authority involves the production of a yellow color by the action of nitric acid, which deepens to crimson on warming, while the ferric chloride reaction—production of a deep red color, nearly discharged by excess of dilute sulphuric acid—is also inserted. This latter test distinguishes antipyrine from other organic substances which produce various colors with ferric chloride and differ in the effect of sulphuric acid upon the color.

Acetanilide has been found admixed with antipyrine. Its detection is very easy, as, though both the compounds have approximate melting points (113° C.), a mixture of equal parts melts at 45° C.

Though a fairly stable body, antipyrine is more or less decomposed or thrown out of solution by a number of other chemical compounds and galenicals—a fact which it is of considerable importance to bear in mind in dealing with mixtures of which it forms an ingredient. From the long lists of drugs and preparations found to be incompatible with the newer substance, the following are taken as more important :—

Acid. hydrocyan. dil.
Acid. tannic.
Butyl-chloral hydras.
Chloral hydras (in strong solution).
Dec. cinchonæ.
Ext. cinchonæ liq.
Ferri sulph.
Ferric salts in solution.
Inf. catechu conc.
Inf. cinch. acid.
Inf. rosæ acid.
Inf. uvæ ursi.
Liq. arsen. et hydrarg. iod.
Mercuric chlor.
Naphtol β (solid).
Nitrites in solution, All acid.
Sodii bicarbon.
Sodii salicylas (solid).
Tinctures containing tannin, iron or quinine.
Tinct. hamamelid.
Tinct. iodi.

Phenyl-urethane and antipyrine liquefy when rubbed together (Suchanek).

Medicinal Uses. Antipyrine is therapeutically a many-sided remedy, playing successfully the role of antipyretic, antirheumatic, antineuralgic and hæmostatic, and being employed against whooping cough, chorea, asthma bronchiale, mal de mer, etc. Externally also it has been applied as an antiseptic, and to a limited extent is applied subcutaneously.

According to Cesari, antipyrine thickens and condenses the blood without coagulating it, and hence its usefulness as a hæmostatic.

The most recent additions to the literature of the use of antipyrine in medicine treat of its value in the diarrhœa of children, in doses of ½ to 1½ grains (Saint-Phillippe); of its

virtue as an antigalactagogue, in 4 grain doses every two hours (Guibert), and of its power in skin diseases, especially in such as are attended by irritation and itching. Dr. Blaschko recommends it in the urticaria-like eruptions of children; the remedy was given in powders, half teaspoonful of a 20 per cent. mixture with sugar, or in solution. The action was so favorable that the author ascribes to antipyrine a direct action on the vascular nerves. Good results were also obtained in urticaria, nervous pruritus, in true prurigo, erythema, pemphigus vulgaris, and lichen ruber. Antipyrine is to be prescribed in such cases mostly as a symptomatic remedy against itching to be assisted by the other usual medicaments. Other favorable experience of the use of the compound in skin diseases is recorded by Prof. Saalfeld.

A powder of antipyrine 15 grains, French chalk 75 grains, boric acid 30 grains and salicylic acid 4 grains has been recommended as an effective remedy in arresting attacks of coryza (Capitan).

In certain cases it seems that antipyrine has a tendency to cause nausea and sickness if taken internally. When this difficulty is met with, it has been recommended to administer the remedy in solution in aërated water, a form for which the free solubility of the antipyretic is a marked advantage (Dujardin-Beaumetz). The same end has been reached by the preparation of compressed tablets of antipyrine with bicarbonate of soda and tartaric acid.

It may be mentioned that the latest observations of the action of antipyrine have led to the expression of the opinion by several authorities that it has a marked, and in some instances dangerous action on the heart, producing lowering of blood-pressure, malaise and collapse (Drasche). To the utterance of warnings to this effect must be ascribed the fact that antipyrine, which was used almost as a specific against influenza during the earlier epidemics, was almost entirely abandoned during the later.

Against the copious perspiration that frequently accompanies the action of antipyrine, atropine or agaricin are given with advantage, either at the same time as the remedy or shortly before it (v. Noorden).

As an antipyretic antipyrine is given in doses of 1¼ to 1½ drachms, in hourly portions of 15 to 30 grains. In phthisis 15 grains are given every time the temperature rises 0.2° C.; in chorea the same dose three times a day. Children are given 1½ grains for every year of age, three times, one after the other, increasing the dose if necessary (Penzoldt).

DERIVATIVES AND ALLIED COMPOUNDS.

Antipyrine being an alkaloidal or basic substance, readily forms compounds of definite chemical nature with acids, which may be regarded as salts of antipyrine. A number of these have been prepared, and are described in literature, but only one of them has been at all generally employed.

Antipyrine benzoate is obtained by the addition of antipyrine to a boiling aqueous solution of benzoic acid. It melts with great readiness; is little soluble in cold or in boiling water, but is very freely so in alcohol and ether. It has a pungent taste, and a slight odor of benzoic acid. The *citrate* and *picrate*, similarly prepared, have also been described.

Antipyrine salicylate, or *Salipyrin*, the only salt of the base which has so far attained any importance, is prepared by the interaction of antipyrine and salicylic acid in substance at 100° C., or in solutions. It occurs as a white, coarsely crystalline, odorless powder, with a rough but not unpleasant sweetish taste; water scarcely takes it up at all, and ether only sparingly, but it is readily soluble in alcohol (also in benzene), from which it crystallizes in hexagonal tables, with a melting point of 91.5° C.

The reaction of sodium salicylate and antipyrine, sometimes stated to be the result of a chemical change, has been decided by careful research to be merely the result of deliquescence, the salicylate acting as a carrier of moisture to the more soluble antipyrine (Spica).

Salipyrin was primarily used in acute and chronic rheumatism, and rheumatic sciatica, with good results (Guttmann, Randozza). Its chief claims to preference are based upon its comparative harmlessness—2½ drms. having been taken within three or four hours without the slightest ill-effect (Hennig)—and freedom from unpleasant by- or after-effects.

Salipyrin was largely used in the epidemic influenza of 1891 to 1892, with satisfactory results (von Mosengeil, Hennig, Schreiner, Speechly, Gogrewe, Althaus). The authorities quoted especially emphasize the freedom of the action of salipyrin from cardiac influence, and see in this feature a marked advantage over antipyrine.

The remedy is administered either in powder (wafers, cachets, etc.) or in mixture, rubbed up with glycerine and flavored with raspberry syrup. In acute articular rheumatism 15 grains are given at intervals of ¼ to 1 hour until about 2 drms. have been taken. In the chronic forms of the disease large doses, beginning with 1¼ drms., are ordered the first day, increasing gradually if necessary. In all rheumatic cases the treatment is continued with smaller doses for weeks or even months after all symptoms have disappeared, in order to prevent relapse. 8 grains is often sufficient to arrest neuralgia. In influenza the dose (8 to 30 grains) is regulated according to the severity of the symptoms.

Antipyrine also forms compounds with phenols, of which two may be appropriately mentioned here, though they have as yet no medicinal importance.

Phenopyrin, prepared from equal parts of crystalline phenol and antipyrine. It is an oily liquid, free from color and odor, insoluble in cold and sparingly soluble in hot water.

Pyrogallopyrin, a crystalline compound obtained by the interaction of pyrogallol and antipyrine, in substance or in solutions. Behaves similarly to the above compound with water, and also like it is readily soluble in alcohol and ether.

Naphtopyrin and *Resopyrin* are described under **Naphtol** and **Resorcin** respectively.

Antipyrine seems to be capable of forming several compounds with chloral (Choay and Béhal). One of these has been brought under the notice of the medical profession as *Hypnal*, readily prepared (Demande) by mixing a solution of 47 grammes (1½ ounces troy) of chloral hydrate in 50 cc. (1½ fluid ounces) of distilled water, with a solution of 53 grammes (1¾ ounces troy, less 22 grains) of antipyrine in 50 cc. of distilled water, pouring into a separating funnel, and drawing off, after an hour, the oily-looking liquid from the

supernatant aqueous layer. At the end of 24 hours the separated liquid will have solidified to a mass of rhombic crystals, and some small rhombs will also have formed in the aqueous liquid. These should be drained and dried on bibulous paper or under a cold dessicator. They are tasteless and odorless, melt at 58° to 60° C., and dissolve in 5 to 6 parts of water.

Recommended as simultaneously hypnotic and analgesic (Bardet), 15 to 30 grains alleviating pain and inducing quiet sleep in troublesome coughs. Prescribed in aqueous mixtures, with some alcohol, flavored with orange and syrup (Bonnet).

Hypnal must not be confounded with **Hypnone** (*q. v.*).

Iodantipyrine, or *Iodopyrine*, is a true substitution product of antipyrine, one atom of hydrogen in the benzene nucleus being replaced by iodine; hence the formula is probably $C_6H_4IN \begin{cases} CO.CH \\ NCH_3.CCH_3. \end{cases}$ The compound crystallizes in tasteless and colorless prismatic crystals, difficultly soluble in cold, but readily so in hot water; melting point 160° C.

The antipyretic activity of iodopyrine exactly corresponds to that of antipyrine; it is decomposed in the stomach into antipyrine and sodium iodide, which produce their separate therapeutical effects (Muenzer). In doses of 8 to 24 grains it reduced the abnormal temperature of typhus and pulmonary tuberculosis without any unpleasant effects; patients felt better during the use of the remedy. Very satisfactory results were obtained in a case of violent (syphilitic?) headache, cured in one day by a single dose of 15 grains, and in another of polyarthritis acuta; the latter patient was able to move about freely six hours after taking the first dose (15 grains). It would appear to be still uncertain whether iodopyrine possesses any advantages over the combined administration of antipyrine and iodide of potassium.

Isonitrosoantipyrine is the name given to the green compound produced by the action of acid nitrites on antipyrine. It was characterized as poisonous, but has been tried in medicine; reports are lacking.

By treating toluol solution of antipyrine with sodium and carbon dioxide a precipitate is formed which according to its

analysis and chemical behaviour (Bruehl and Koebner) is an *Antipyrine alcohol*, with the formula $C_{11}H_{14}N_2O$. It melts at 144 to 145° C. when pure, crystallizes in prisms, is readily soluble in ethyl and methyl alcohol in chloroform, benzene, and acetic ether, but difficultly so in water and ether. Therapeutically this body has not yet been examined.

ARISTOL.

Synonyms: DITHYMOLDIIODIDE, ANNIDALIN.

$$\left.\begin{matrix}C_3H_7\\CH_3\end{matrix}\right\}C_6H_2(OI)C-C(OI)H_2C_6\left\{\begin{matrix}C_3H_7\\CH_3\end{matrix}\right.$$

A somewhat unstable amorphous powder, believed to result from the condensation of two molecules of thymol, and the substitution of the hydrogen of the OH group and of one CH group in each by iodine. It contains about 46 per cent. of iodine. It was first introduced under the name *Annidalin*, but subsequently rechristened and again brought out.

Preparation.—Aristol may be prepared by the decomposition of a solution of iodine in iodide of potassium by an alcoholic solution of thymol. In order to insure uniformity of result many precautions have to be taken, as aristol does not seem to be the product of very well defined chemical action.

Physical and Chemical Properties.—A brownish red, odorless, amorphous powder, insoluble in water and glycerine, slightly soluble in alcohol, and readily in ether and collodion; also taken up by fatty oils when rubbed together with them, and by vaselin. Aristol is easily decomposed by light and heat, and hence all solutions should be made without the aid of the latter, and kept from the action of the former force.

When heated in a glass tube violet iodine vapors are given off. When dried for an hour at 90° C. aristol should lose at most 1 per cent. of moisture. The aqueous extract should be neutral to litmus (absence of free alkali), leaving no residue on evaporation, and giving no blue color when fuming nitric

acid and starch paste are added (absence of sodium iodide). An extract with 1 per cent. iodide of potassium solution should be colorless and give no violet or blue tint with starch paste (absence of free iodine).

Soon after its introduction, Langgaard stated that aristol gave up iodine with great readiness to substances with an affinity for it, and pointed out that thereon depended certain restrictions in its use.

Recently manufactured specimens of this compound have been found to be less contaminated with free iodine than earlier batches, but it still contains alkaline iodide (Reuter). It may be purified from the latter by solution in glacial acetic acid, precipitating with water, thoroughly washing the precipitate, and drying at 60° C. The pale yellow product dissolves clearly and without residue in ether, and also contains no free iodine. There seems however some doubt as to the activity of this purified form. (*v. infra.*)

Medicinal Uses.—Aristol was introduced as a substitute for iodoform, over which it has the advantage of being odorless. It seems possible that the success first attained by the use of the remedy in ointment form against skin diseases was in part due to the less care taken in preparing it free from uncombined iodine and from soluble iodides. At any rate doubt has recently been thrown upon the efficacy of perfectly pure and, therefore, fairly stable aristol. Probably in the same direction lies the explanation of the unsatisfactory results sometimes obtained, such as those of Prof. Neisser, who found the substance quite inactive save in some cases of lupus, where it followed the application of a caustic.

The first observer, Eichhoff, characterized aristol as second only to iodoform in the treatment of indolent soft ulcers, and obtained in lupus such remarkable results that he believed it to be a specific poison for the bacillus of tuberculosis, while at the same time it stimulated the growth of fresh granulations. The experience of other observers in this disease was less satisfactory (Neisser, Schirren). It gave good results in the treatment of psoriasis (Schirren), a specially useful form being a 10 per cent. solution in flexile collodion (Schuster). In the ulcerative processes of syphilis, and in all cases where iodo-

form had been used, e. g., in gynæcology, dermatology, diseases of the ear, nose, pharynx, etc., aristol did good service in the hands of medical men in the principal countries of Europe. Quite recently it has been well spoken of in diseases of the ear and nose (Buerkner), in eczema and mild psoriasis (Weissblum), and in severe burns (Stern).

It has been already intimated that some authors have not been so favorably impressed by the action of the compound; it has an undoubted advantage over iodoform in being odorless, but it appears to be inferior to it in activity (Heller).

The most suitable forms for applying aristol, besides the powder, are solutions in oil or ether (5 to 10 per cent.), a zinc-starch paste—which remains unchanged, though the compound is decomposed by admixture with substances having a strong affinity for iodine (Langgaard),—or ointments with lanolin or with vaselin (5 to 10 per cent.), prepared by carefully mixing the ingredients on a slab, warming gently while assiduously stirring and straining. The liquid vaselin exerts a solvent action upon the aristol, and thus a smooth ointment results. For gynæcological application suppositories have been ordered containing 8 to 15 grains of aristol each with cacao butter. A liniment, made by dissolving 5 grns. of aristol in 2 drms. of a mixture of equal parts of ether and alcohol, and incorporating 1 oz. of soft soap, is also useful in certain cases.

Apparently the prolonged employment of aristol may sometimes gives rise to chronic iodine poisoning; cases have been recorded, in which a decidedly cachectic condition was observed in patients under the treatment, which disappeared when the use of the remedy was suspended (Ewald).

DERIVATIVES AND ALLIED COMPOUNDS.

Cresol iodide, or *Iso-butyl-phenol iodide*, a compound recently announced as likely to be introduced into medicine, is prepared by a method exactly analogous to that adopted for aristol, and on the whole it closely resembles the latter in its properties. By the use of ortho, meta, or para-cresol the corresponding isomeric iodides are obtained. (See also under Cresols).

BENZANILIDE.

Synonym: BENZOYL-ANILIDE.

$C_6H_5NH\ COC_6H_5$.

A crystalline compound bearing the same relation to benzoic acid as acetanilide to acetic acid.

Preparation.—By the action of benzoyl chloride or of benzoic anhydride on aniline, the reaction being thus represented:—

$$\underset{\text{Aniline}}{C_6H_5NH_2} + \underset{\text{Benzoyl chloride}}{C_6H_5COCl} = HCl + \underset{\text{Benzanilide.}}{C_6H_5NH\ C_6H_5CO}.$$

Physical and Chemical Properties.—Colorless, micaceous, lustrous, scaly crystals, insoluble in water, soluble in alcohol. Melting point 163° C.; at a higher temperature distils unchanged.

Medicinal Uses.—First commended by Cahn and Hepp as an antifebrile specially suitable for children; the dose being 3 to 8 grains, according to age; and later by Kahn, of Frankfort. It produced exanthema sometimes, and apparently had not sufficiently marked advantages to insure its retention in materia medica; at any rate nothing has been added to the literature of benzanilide for a considerable time.

BENZOSOL.

Synonym: BENZOYL-GUAIACOL.

$C_6H_4OCH_3OCOC_6H_5$.

A crystalline compound of guaiacol in which the hydrogen atom of the hydroxyl is replaced by benzoyl.

Preparation.—By formation of a potassium salt from crude guaiacol and purification of the salt by re-crystallization from alcohol. The pure product is then warmed with the calculated amount of benzoyl-chloride, and the resultant benzosol re-crystallized from alcohol. Also by the interaction of guaiacol with benzoic anhydride.

Physical and Chemical Properties.—A colorless crystalline powder, almost odorless and tasteless. Melting point 50° C. Insoluble in water, readily soluble in hot alcohol, in

ether and in chloroform. It contains 54 per cent. of guaiacol. The melting point of benzosol should not be below 44° C. (Bongartz), and when allowed to remain in contact with sulphuric acid, even for prolonged periods, only a pale yellow coloration should be produced. When saponified with alcoholic potash a pure guaiacol odor should be developed. Benzosol is distinguished from salol by the fact that it gives a purple-red color when treated with concentrated sulphuric acid in the presence of acetone, whilst salol assumes a yellow color with a shade of red.

The products of the decomposition of benzosol in the organism (its constituents) can be readily detected in the urine and saliva of patients under treatment (or even half an hour after a single dose); the secretion is distilled with diluted sulphuric acid, the clear distillate (in which the guaiacol can be detected by the sense of smell) is placed in a test tube, and to it is added a small quantity of a highly dilute solution of liquor ferri sequichlorati (2 to 3 drops to a test tube full of water). In the presence of guaiacol a reddish-brown color is gradually developed, the intensity of which is proportional to the amount of the compound in the solution. It can be detected by the same method in the perspiration.

Medicinal Uses.—The therapeutical value of benzosol in the treatment of phthisis depends upon its content of guaiacol, which appears to be set free by the alkaline juices of the intestinal tract, being excreted as combinations of guaiacol and benzoic acid with the urine. Its advantage over the parent substance (guaiacol) is of course its comparative freedom from taste, so that it can be given in large doses—an essential of the so-called intensive guaiacol treatment of phthisis—without the disturbance of the digestive functions or disagreeable eructations caused by the former as liquid in mixtures, while at the same time free from the local irritant effect sometimes ascribed to the capsules, and superior to pills in readiness of absorption.

In doses of 4 grains, gradually increasing to 12 grains, three times a day (equal to about 24 grains of creasote), results were obtained in the treatment of phthisis equal if not superior to those yielded by creasote (Walzer). The action of the

remedy in ten closely observed cases soon manifested itself in a decrease of the number and violence of the fits of coughing, a diminution in the expectoration, and disappearance of hectic perspirations. The appetite, and with it the general condition and well-being, speedily improved, as was evidenced by the increase of body-weight.

The compound was given in powder, in pastilles of sugar and chocolate, or with addition of oil or spirit of peppermint.

Benzosol has been put upon the market by more than one firm, and there is reason to believe that the products are different. At least, one of them is reported by Professor Sahli to have a different smell and odor to that described above, and this in large doses (1½ to 2 drachms daily) and with continued use had no effect at all upon the disease. Sahli concluded that the effects of guaiacol and creasote were due to local antiseptic action in the stomach, and hence would not be substituted by benzosol, but this view is not supported by the experience of others with the treatment. (*Cf.* **Guaiacol**—*Medicinal Uses.*)

BETOL.

Synonyms: Naphtalol; Naphtosalol; Salinaphtol.

$C_6H_4OH\ COOC_{10}H_7$.

A crystalline compound, with the composition of a β-naphtol salicylate, and closely allied to salol.

Preparation.—By heating together a mixture of β-naphtol-sodium, sodium salicylate and phosphoric chloride; besides betol, sodium meta-phosphate and sodium chloride are formed.

Physical and Chemical Properties.—When pure, betol forms a colorless, odorless and tasteless, lustrous, crystalline powder, melting at 95° C. Insoluble in water or glycerine, soluble with difficulty in alcohol and turpentine, readily in boiling alcohol (1 : 3), ether, benzene, and in warm linseed oil.

Betol is a fairly stable body, unaffected in the cold by alkalies or acids (unless very strong); when heated with these reagents in strong solutions it splits up into β-naphtol and

salicylic acid. The same effect is produced by the alkaline pancreatic juice and other intestinal ferments, but the acid secretions of the stomach have no effect upon it. It appears in the urine as salicylic acid and naphtol glycuronate.

Absence of free salicylic acid is proved by pouring a few drops of an alcohol solution into very dilute ferric chloride solution, when no color should be produced. The compound is distinguished from salol by its much higher melting point (salol = 43° C.), and by the production of a pure lemon-yellow colored solution with pure concentrated sulphuric acid, which a trace of nitric acid changes to olive brownish-green. With salol no such color results.

Inorganic impurities, chlorides, phosphates, etc., are detected in the usual manner. Impure preparations are said to assume a blue or reddish tint on keeping.

Medicinal Uses.—At first it was expected that betol would prove equally as valuable as salol, but its higher melting point and chemical stability proved to be disadvantages which restricted its use. At the same time its lower degree of solubility also told against it, and although it was used internally as powder in vesical catarrh, articular rheumatism, etc. (5 to 6 grains four times a day), instead of sodium salicylate (Kobert), and externally in the form of bougies (1 : 4 of cacao butter) in the treatment of gonorrhœa, it seems now to have been almost entirely forgotten.

BROMOFORM.

Synonym : Tribromomethane.

$CHBr_3$.

An analogue of chloroform, discovered in 1832 by Löwig.

Preparation.—By the action of bromine upon a solution of equal parts of caustic potash and methyl alcohol. The separated bromoform is washed with sodium carbonate solution, freed from water with calcium chloride, and rectified.

Just as iodoform and chloroform have recently been prepared from acetone, so a process has been devised (Denigès)

for the production of bromoform. Bromine is added to soda solution artificially kept cool; bromide and hypobromite of sodium are formed thus:

$$6\,Br + 6\,NaHO = 3\,NaBr + 3\,H_2O + 3\,NaOBr$$

Sodium hypobromite.

Acetone is then brought into contact with the mixture when (even in the cold) reaction takes place, the by-products being acetate and hydrate of sodium:

$$3\,NaOBr + CO(CH_3)_2 = CHBr_3 + CH_3COONa + 2\,NaOH$$

Acetone — Sodium acetate.

The yield amounts to about 60 to 70 per cent. of the theoretical quantity.

Physical and Chemical Properties.—A clear, colorless liquid when pure, with a peculiar but not unpleasant odor, and a sweet taste. Specific gravity 2.9, and boiling point 147 to 148° C., (149 to 150° C. Denigès). Bromoform is only very slightly soluble in water (8 or 10 drops in 6 ounces of water), but readily in alcohol. When evaporated by gas or lamp-light, bromine and a bromine compound ($COBr_2$)—very irritating to the mucous membrane of the throat and conjunctiva—are apparently produced, analogous to the chlorine and phosgen gas formed from chloroform under similar conditions.

Bromoform for medicinal use must be free from acid and color. Yellowish specimens are unfit for administration until they have been purified by washing with dilute soda solution and drying over calcium chloride. Pure bromoform also does not attack the mucous membrane like chloroform. It must be kept out of sunlight.

Medicinal Uses.—Bromoform was warmly recommended in 1889, as a remedy for the whooping cough of children, in daily doses of 5 to 20 drops, dissolved in 4 ounces of water with addition of spirit.

℞ Bromoformi.... ..... gtt. x.
Spir. vini rect..... ♏ 45 to 60
Syrupi..... q.s.
Aquæ dest..... ad. ℥iv.
M. S. To be taken during the day.—(Stepp).

The same author afterwards prescribed the remedy unmixed, so many drops being ordered to be taken in water, coffee, or the like. Equally favorable results were obtained by others (Senator, Lœwenthal, Schippers, Cassel), and from the experience of some hundreds of cases, bromoform was pronounced to be harmless, and to have a marked effect in promptly diminishing the number and violence of attacks, the excretion of mucus and the duration of the disease, while also vomiting and bleeding from the mouth and nose were arrested. According to Neumann, the action is very often good, but the remedy is no specific.

The pleasant taste of the compound—an undoubted advantage in the treatment of children—has also proved a source of danger. Cases have been described in which the little patients, tempted by the nice flavor of the medicine, obtained access to the bottle and drank the whole contents, equivalent sometimes to 20 or 30 drops of bromoform. Deep narcosis supervened, preceded by a short stage resembling alcoholic intoxication. Injections of ether in one instance, and fresh air with prolonged practice of artificial respiration in another, were eventually successful, and the patients on recovery felt quite well. It is evident that the dosage should be carefully restricted, and it would seem advisable not to adopt the practice of sending out the unmixed bromoform.

According to recent researches on animals inhalations of bromoform have an anæsthetic effect similar to that of chloroform (Rabuteau); the narcosis seems however to be of shorter duration.

Good results have been recorded from the external application of the liquid as an analgesic and antiseptic (Solis Cohen). Ozæna and tuberculous and other ulcers of the larynx were successfully treated by the local use of bromoform, the affected areas having been previously cleansed by hydrogen peroxide. As the substance is volatile the effect was transient, and the author recommends to follow with the application of iodoform.

BROMOL.

Synonym: Tribromophenol.

$C_6H_2Br_3OH$.

A compound well-known to the chemist, being produced in one of the processes used for the estimation of phenol or carbolic acid.

Preparation.—When dilute solutions of phenol are precipitated with bromine water a crystalline precipitate is formed, consisting of carbolic acid in which three atoms of hydrogen in the benzyl group and that of the hydroxyl group are replaced by bromine; on solution in alkali, and reprecipitation with acid, tribromophenol is formed.

Physical and Chemical Properties.—When pure, bromol forms white crystals, melting at 95° C., practically insoluble in water, but freely taken up by alcohol, ether, and chloroform; also soluble in glycerine, in fatty and essential oils. The odor is unpleasant, bromine-like, and the taste sweetish-astringent.

Tribromophenol was bacteriologically investigated by Grimm, in 1888. "Bromol" is recommended to be used in solution (1 : 30 olive oil) or ointment (1 : 10), as powder or dressing. Against diphtheria a 4 per cent. glycerine solution is to be used. In doses of one-tenth to one-third grain it has been given in cholera infantum and typhus abdominalis as an intestinal disinfectant.

DERIVATIVES AND ALLIED COMPOUNDS.

Chlorphenol. Under this term a liquid, described as very volatile, and giving off vapors specifically heavier than air, has been recommended for inhalation in pulmonary tuberculosis and other diseases of the respiratory organs. The inhalation liquid consists of 7 parts of a chlorinated phenol (probably orthomonochlorphenol) and 3 parts of a mixture of alcohol, eugenol and menthol; 16 to 30 drops are inhaled daily, the heavy vapors penetrating into all recesses of the lungs, and there exerting their antiseptic action (Passerini). Chlorphenol has also been used as an application to wounds, indolent ulcers, etc. Cures are recorded from the treatment in 5 cases of incipient pulmonary tuberculosis (Passerini).

CHINOLINE.

C_9H_7N.

A tertiary amine, first prepared by the distillation of quinine or of cinchonine, and subsequently synthesised by Bayer, Königs, and others.

Preparation.—Either by extracting the elements of water from hydrocarbostyril with phosphorus pentachloride, or by the action of caustic soda upon the mixture of acrolein, nitrobenzol and aniline, formed when nitrobenzol, aniline, glycerine and sulphuric acid are heated together. The chinoline obtained is purified by fractionation and precipitation from alcoholic solution as sulphate, or by ebullition with chromic acid.

Physical and Chemical Properties.—Pure chinoline is a colorless liquid with a pungent characteristic aromatic odor. Specific gravity at 15° C., 1.084; boiling point 237° C. Very slightly soluble in cold water (though hygroscopic), more readily in hot water, and freely in alcohol, ether and chloroform. By the action of light and air chinoline is rapidly turned brown; it is decolorized by shaking with solid potash or soda and slow rectification. Chinoline by direct addition of acids forms crystalline salts which are mostly hygroscopic, and double salts with the metals. By the action of fuming sulphuric acid the base is converted into chinoline sulphuric acid, which, when melted with potash, yields oxychinoline, C_9H_6NOH.

Evidently the compound may be contaminated by water (which lowers the melting point), by homologous compounds (which raise it), by aniline or nitrobenzol and hydrocarbons. Aniline, if present, gives a violet color with chlorinated lime solution, and nitrobenzol or the hydrocarbons separate as oily drops when the base is mixed with excess of concentrated sulphuric acid and cooled.

Medicinal Uses.—Chinoline is antiseptic, antizymotic and antipyretic (Donath); 0.2 per cent. prevents the putrefaction of urine, 0.4 per cent. that of blood. Subcutaneously injected into animals it lowered the body heat; doses of 15 to 30 minims *pro die* were recommended for human beings, but not much employed. Has been found useful for

local application in pharyngology (Seifert), and for the disinfection of the cavities left after the extraction of carious teeth (Scheff). Cotton wool is soaked in pure chinoline, pressed into the canal, allowed to remain 24 hours and renewed; perfect asepsis is attained in two or three days.

DERIVATIVES AND ALLIED COMPOUNDS.

Chinoline bisulphate, hydrochloride, salicylate, tannate and tartrate have been recommended. The two chief salts are described below:

Chinoline salicylate, a white crystalline powder, soluble in water (1:8) and in glycerine; very soluble in alcohol, ether, vaselin, and fatty oils.

Chinoline tartrate occurs in long white rhombic crystals, with a faint amygdaloid odor; it has the advantage over most chinoline salts of being non-hygroscopic. 70 to 80 parts of cold water are required for solution, but less of hot water. In 5 per cent. solution, it has been successfully employed in whooping cough (1½ grns. every three hours—Koch and Seifert), and in doses of 15 grains, in two or three portions, three hours before the attacks, in intermittent fever (Loewy). According to Brieger, however, chinoline has no useful action, but on the contrary irritates the stomach.

Kairin, or ethyl-kairin, $C_9H_{10}(C_2H_5)NO\,HCl$, prepared from chinoline, through α-chinoline sulphonic acid, α-oxy-chinoline and α-oxychinolinetetrahydride, was one of the first substitutes for quinine prepared by synthesis. It was recommended by Filehne, in hourly doses of 5 to 8 grains, or single doses of 15 grains, as an antifebrile, but its use was attended with considerable risk; subsequently it was displaced by the antipyretics later discovered, and now is no longer manufactured.

The so-called *Kairin M.* was hydrochloride of α-oxychinolinemethyltetrahydride, $C_9H_{10}(CH_3)NO\,HCl$, whilst *Kairolin A.* and *Kairolin M.* were the acid sulphates of ethylchinolinetetrahydride and methylchinolinetetrahydride respectively.

Ortho-oxyethyl-ana-mono-acetylamidochinoline is the sounding name by which a new antipyretic was announced some months since. M. p. 155° C., readily soluble in hot water, difficultly so in cold; freely taken up by alcohol and dilute acids.

CHLORALAMIDE.

Synonym: CHLORAL-FORMAMIDE.

$CCl_3CH.OH.CONH_2$.

Preparation.—By the interaction of chloral (not chloral hydrate) and formamide, according to the equation

$$CCl_3CHO + CHONH_2 = CCl_3CH.OH.CONH_2.$$

Chloral. Formamide. Chloralamide.

Physical and Chemical Properties.—Lustrous, colorless crystals, with a somewhat bitter taste. Melting point 115° C.; at a higher temperature it dissociates into its components. Slowly soluble in about 20 parts of cold water, or in 1½ parts of 96 per cent. alcohol. By water heated over 60° C. it is decomposed into chloral hydrate and ammonium formate, and the same effect is produced by the action of alkalies, but not by dilute acids.

Medicinal Uses.—Chloralamide was recommended by von Mering as a substitute for chloral hydrate, being slowly decomposed into its constituents in the blood, when the formamide by its stimulant action upon the vascular centres counteracted the fall of blood pressure brought about by the chloral. The compound has been largely and widely adopted as a hypnotic, on the whole with very satisfactory results (Kny, Reichmann, Hagen and Hüfler, Rabow, Alt, Patterson, White, Strahan, Gordon, Atkinson), the authors agreeing that the remedy has no injurious action on the heart, that it is effective even when the patients are suffering from painful diseases, and that the sleep produced is light and refreshing. Some of the observers named regard chloralamide as "the ideal hypnotic, free from all unpleasant or dangerous by- or after-effects" (Atkinson).

Physiological research has shown: 1. that chloralamide acts more powerfully upon the cerebral cortex than upon any other portion of the nervous system of voluntary life, thereby causing sleep and muscular relaxation; 2. that in moderate doses it stimulates the respiration; and 3. that it has a very feeble influence upon the circulation (Wood). Its physiological action has also been described as exactly similar in kind to that of chloral hydrate (Mairet and Bosc).

Evidence is abundant that in practice there is a real distinction between the effect of the older hypnotic and its newer derivative. Cases are recorded, in which the nervous system, "almost entirely wrecked," has been improved in tone by the quiet refreshing slumber induced by chloralamide, where chloral hydrate had failed (Mattison).

Very satisfactory results have been yielded by chloralamide in the treatment of the insomnia of alcoholism (Helm and Hexamer), of mental disorders generally (Naecke, Wright, Umpfenbach), in gynæcology (Denhard, Dupon), especially in aggravated cases with hysterical convulsions, in senile insomnia, pulmonary diseases, neuralgia, and hysteria (Gordon, Charteris, Therapeutic Committee of the British Medical Association).

That the remedy may be given with safety, even when the heart is affected, is demonstrated by a number of cases. In one of them the patient (an old lady of 60 years) had suffered from heart disease for eight years, and was troubled with dyspnœa, cough and insomnia. Morphine was first tried without any great benefit, and than chloralamide was given in 10 grain doses, gradually increased to 40 grains. Better and longer rest was thus obtained, and the pulse improved (Patterson).

Chloralamide is useful to quiet the nervous system, and to produce sleep after major operations. For this purpose it is "the ideal sedative, giving prompt and satisfactory action, without the disadvantages of chloral, morphia, and other narcotics" (Lanphear).

A recent publication from America deals with conclusions based on the treatment of nearly 300 cases with chloralamide, given in a mixture similar in strength to that cited below (but containing tincture of cardamoms for spt. frumenti, and syrup of orange as well as of raspberries). The conclusions are eminently favorable and confirm those of the other authors who recommended the remedy (J. Wood).

Subcutaneously administered (4 per cent. aqueous solution) quiet and refreshing sleep, lasting for about eight hours, was induced by one or two syringefuls (each of 15 minims) in

carcinoma of the rectum with violent pain, and in severe hepatic colic (E. Schmidt).

The dose of chloralamide is 15 to 40 grains, and it should be prescribed and dispensed only in solution. Further, it is necessary to point out that as hot water decomposes the compound it must always be dissolved in the cold. The addition of spirit, in which chloralamide is freely soluble, facilitates the preparation of mixtures. An approved formula is:

℞ Chloralamidi ..... ℥ ii
Spt. Frumenti ..... ℥ i
Ft. solut. et adde
Syr. Rubi idæi ..... ℥ i
M. S. One tablespoonful, to be repeated in one hour if sleep be not produced.

Any flavoring syrup may be substituted for the syrup of raspberry, or glycerine and tincture of ginger, or cardamoms, or an aromatic water may be added. The liqueur "Bénédictine" (1 to 2 drms. to each ounce of water) is also a good and agreeable corrective (Atkinson).

Chloralamide may be effectively prescribed in solution with bromide of potassium (Charteris).

DERIVATIVES AND ALLIED COMPOUNDS.

Chloralammonium.—A white crystalline powder consisting of small needles, with a melting point between 62° and 64°C.; soluble in water, but the solution is very prone to change. The substance is said to be split up even in the solid state. Has been given as a hypnotic in doses of 15 to 30 grains, and is described as combining the properties of urethane and chloral hydrate, but having a less marked action on the heart and respiratory centre than the latter (Nesbitt).

Chloral-urethane and *Ethylated Chloral-urethane*, or *Somnal*, *vide* **Urethane.**

Chloralimide is a chloral derivative, prepared by the action of heat on chloralammonium. The formula of this compound, (which must not be confounded with chloralamide), is given as CCl_3CHNH; it occurs in long crystalline needles, without color, taste or odor; melting point about 166° C.; insoluble in water, soluble in alcohol, and more in ether, in chloroform and in fatty oils. Chloralimide is very stable,

being unaffected by light, air or moisture. It was introduced as a substitute for chloral hydrate, to which it was said to be superior in activity (Choay), but it has been practically discarded and is no longer prepared.

CRESALOLS.

Synonyms: Cresol Salicylates. Cresolsalols.

$C_6H_4OH\ COC_6H_4\ CH_3$.

Ortho-, meta-, and para-cresalol are crystalline esters, analogous to betol and salol.

Preparation.—By heating together at a high temperature molecular weights of the salicylate, and of the cresylates of sodium with phosphoric chloride, a cresalol (ortho, meta or para according to the sodium salt used) is formed as well as sodium chloride and phosphoric anhydride. The product is treated with water which removes the sodium salt and the phosphoric anhydride, and the cresalol is purified by repeated crystallisations from alcohol.

Physical and Chemical Properties.—All three isomeric cresalols are bulky, white crystalline powders, with a salol-oid odor. They are insoluble in water, readily soluble in alcohol and in ether, and slightly taken up by oils. Ortho-cresalol melts at 35° C., meta-cresalol at 74° C., and para-cresalol at 39° C.

Medicinal Uses.—The employment of these "esters" in medicine depends upon the readiness with which they are split up in the organism into their components, cresol and salicylic acid, thus exerting a powerful and searching antiseptic action. As the cresols are more powerful antiseptics than carbolic acid, and at the same time are less poisonous and more mild in their physiological effects (Frænkel), the cresalols would seem fitted to play an important role in intestinal antisepsis. Nencki recommends the para form for that purpose, believing it to be superior to and safer than salol. The cresalols may be usefully given in articular rheumatism and vesical catarrh, in daily doses of 1 to 2 drachms in divided portions (Sahli).

The antiseptic properties of the compounds have also been utilized externally. The experiments of Birscher showed that for this purpose the meta variety is most suitable, since, used as a dusting powder, it does not "ball," its melting point being some distance above the body temperature. Poisoning symptoms were not noticed with the compound, while it seemed to lessen the secretion of wounds more than iodoform, besides being odorless.

CRESOLS.

$$C_6H_4 \begin{cases} CH_3. \\ OH. \end{cases}$$

The cresols occupy the second place in the homologous series of univalent phenols.

Preparation.—By fractional distillation from coal tar, being contained in the portion which goes over between 200° and 210° C., or from the toluidines by replacing the group NH_2 by OH, or from the toluol sulphonic acids by fusion with potash.

Physical and Chemical Properties.—Ortho-cresol melts at 31°C., and boils at 188°; meta-cresol is a thick liquid which boils at 201° C., but does not solidify even at –80° C.; para-cresol forms colorless prisms which melt at 36° C. and boil at 198° C.; it has a phenoloid odor, and is difficultly soluble in water. Like the other varieties it gives a blue color with ferric chloride.

Medicinal Uses.—It was early discovered that the cresols possessed wonderful antiseptic properties, while at the same time far less poisonous to the animal organism than carbolic acid or phenol (Frænkel). A serious hindrance to the employment of this germicidal activity existed however in the insolubility of the compounds, and for this reason they found no application for a considerable time. During the past year or so attention has again been directed to the solution of the cresols in such a way as to make them available as antiseptics and disinfectants, and a number of preparations have recently been brought under the notice of the

medical profession, consisting practically of solutions of the cresols. The more important are described below as

DERIVATIVES AND ALLIED COMPOUNDS.

Creolin.—This was the first form in which the cresols were presented in a liquid condition for use in medicine. It is a dark-brown alkaline liquid, which forms a more or less turbid milky mixture or emulsion with water, having the characteristic odor of the preparation. With chloroform, ether, and absolute alcohol it mixes in all proportions.

Being relatively non-poisonous,—considerable quantities having been taken without fatal issue,—and free from caustic or even irritating properties, creolin has been largely adopted in surgery as an antiseptic. Its powerful germicidal and deodorant properties were established in the laboratory, bacteriologically (v. Esmarch, Eisenberg, Frœhner, Haenle, Washbourn and others) and practically in surgical practice by a very large number of authorities. The literature refers to its use externally in every department of antiseptic surgery with good results, and to its administration internally in gastric fermentation, dysentery, typhoid and the like, against phthisis (Neudoerfer, Blake), leucorrhœa, gonorrhœa, vesical catarrh (Kortuem).

Quite recently creolin has done good service in acute dysentery of a typhoid character, in colitis and entero-colitis (Watson), being applied in the form of an enema containing 5 per mille of the remedy. All the cases promptly recovered. Also recommended against epidemic influenza (Rabener).

Creolin is employed pure, in solution (1 to 2 per cent.), in ointment form with lanolin *(Lano-creolin)*, as a dusting powder, gauze and surgical soap (all 10 per cent). Internally it is administered in capsules containing 5 minims each.

Lysol.—This preparation is made by dissolving in fat, and subsequently saponifying with the addition of alcohol, the fraction of tar oil which boils between 190° and 200° C.; it is a brown, oily-looking, clear liquid, with a feebly, aromatic, creasote-like odor. Described as containing 50 per cent. of cresols; miscible with water, forming a clear, saponaceous,

frothing liquid; also with alcohol, petroleum spirit or benzin, chloroform, carbon bisulphide and glycerine.

As the chief advantage of lysol its solubility in water is claimed; this renders it specially suitable for the immersion of instruments, since they can be taken out with ease as required. The saponaceous character of the solutions is also advantageous in many cases—rendering a special surgical soap unnecessary—but for the handling of small instruments or the tying of fine threads the hands and instruments must be dried with a sterilized towel.

Experiment has shown lysol to be five times stronger than carbolic acid, and eight times less poisonous (Cramer, Wehmer). It does not attack the operator's hands, but renders the skin soft and supple (Haenle). Used and recommended in gynæcology and general surgery (Cramer, Wehmer, Michelsen, Haenle, Pée, VonderGoltz), in skin diseases (Unna), especially in lupus (Leslie Phillips), and in veterinary practice (Straube).

Solveol and *Solutol.*—The slipperiness which the saponaceous solutions of the cresols give to the hands and instruments has been already referred to as sometimes inconvenient. Researches recently carried forward, with the view of finding other means of preparing neutral aqueous solutions, showed that the salicylates, all salts of oxybenzenecarboxylic acids, of oxybenzenesulphonic acids, of benzo-benzoic acid, and of benzenesulphonic acid, as also the similar derivatives of naphtalene, possessed the property of dissolving the cresols. Solveol is such a solution of sodium-cresol in excess of cresol, and solutol a solution of cresol in cresotate of sodium. Bacteriological experiments with the solutions indicated that they were suitable for application in surgery as dilute solutions (0.5 per cent.), said to be approximately as poisonous as those of pure carbolic acid. Preferable to acid solutions as they do not attack metal.

Paracresol.—Early in the year 1892 patent-rights were sought for a disinfectant, introduced in Germany under this name, to which the formula $C_6H_4 \left\{ \begin{matrix} CH_3 & (1) \\ OH & (4) \end{matrix} \right.$ was ascribed. It was said to give with water in every proportion a pure,

neutral, non-caustic, almost odorless solution, similar to that of carbolic acid, but more active and safer; from these characteristics it is evident that the substance was not the unmixed chemical compound known to the chemist as paracresol (*v. supra*). Recommended in aqueous solution with glycerine for applying to the skin when peeling in various infectious diseases, for the use of midwives as a preventive of puerperal fever, etc.

Cresol iodide.—A fine, very light powder of yellow color, and fairly strong, not very pleasant, odor. Very readily soluble in alcohol, ether, chloroform, and especially in fatty oils; insoluble in water. Rubbed between the fingers it has a resinous feel, and adheres to the hands and instruments so that they can be cleaned only with alcohol. In the organism mere traces of iodine are set free, so that the risk of poisoning is regarded as reduced to a minimum. Has proved useful in diseases of the nose (Petersen, Szoldeski).

Other cresol salts await the attention of the physiologist and therapeutist, among which are various *Cresol cresotates*, such as *m*-cresol *o*-cresotate (melting point 57° C.), *p*-cresol *p*-cresotate (melting point 75° C.), and certain *Phenol cresotates*, as phenol *m*-cresotate (melting point 47° C.), and phenol *p*-cresotate (melting point 93° C.).

CRESOTIC ACIDS.

Synonyms: Homosalicylic Acids; Oxytoluic Acids.

$C_6H_3CH_3OHCOOH$.

These compounds, of which three are distinguished as ortho-, meta- and para-cresotic acids, are homologous with the ortho-, meta-, and para-oxybenzoic acids.

Preparation.—By the interaction of sodium and carbon dioxide and the three isomeric cresols, according to the well-known Kolbe's method of synthesising salicylic acid. They may also be prepared (1) by melting sulphonic acids of the aromatic series $C_nH_{2n-8}O_2$ with caustic alkali; (2) by melting

the homologues of phenol with excess of potassium; (3) by the oxidation of their aldehydes, and, (4) by the substitution of an hydroxyl group in the phenoene nucleus of the toluic acids.

Physical and Chemical Properties.—These three cresotic acids crystallize in long white prismatic needles, volatile in steam. They are very difficultly soluble in cold water, somewhat more so in hot, and readily in alcohol, ether, and chloroform. They have different melting points; viz., ortho, 160° C.; meta, 177° C.; and para, 151° C. Their aqueous solutions are colored violet by ferric chloride, and in other reactions they exhibit a resemblance to the salicylic acids.

Medicinal Uses.—The cresotic acids themselves have not been employed in medicine. Physiological experiments exhibited considerable differences between the three isomeric modifications, the ortho being a pronounced heart-poison, the meta practically inert, and the para intermediate in actions being less poisonous than salicylic acid (Demme). Since thes, researches, carried out in 1888, the salts of the para variety alone have been employed in medicine.

DERIVATIVES AND ALLIED COMPOUNDS.

Sodium cresotate.—A substance so called was used as an antipyretic so far back as 1876–9 (Buss, Koranyi, Gatti), bue in the latter year was found to be a mixture of chiefly *p*-cret sotate of sodium with variable quantities of the *o*- and *m*-compounds. The use of salts of the cresotic acids seems to have been then abandoned until the introduction of the definite

Sodium paracresotate, a finely crystalline white powder, with a bitter but not repulsive taste; soluble in 24 parts of warm water, the solution not separating on cooling. Used as an antiseptic and in the treatment of rheumatism, and considered superior to the salicylate in the absence of disturbing effects upon the digestive organs (Demme, Fraser). Extended physiological research proved that paracresotate of sodium is less poisonous than the salicylate, and that from 8 up to at least 45 grains can be taken daily for several days in succession without ill effect (Henne).

The dose recommended is about 1¼ to 1½ drachms *pro die*, in four or five divided portions; for children the daily dose is 8 to 40 grains, prescribed in mixture with syrup, brandy, or small doses of tincture of opium.

DITHIOSALICYLIC ACIDS.

Synonyms: Di-β-thiooxybenzoic Acids.

$HO_2C(OH)C_6H_3S - SC_6H_3(OH)CO_2H$.

Some nine isomeric substances of the composition indicated above seem to be possible, of which two have been introduced into medicine in the form of sodium salts distinguished as No. I and No. II.

Preparation.—Equal molecular weights of salicylic acid and sulphur chloride are heated to 120° to 150° C.; reaction takes place according to the equation

$$2\,C_6H_4\begin{cases}OH\\COOH\end{cases} + 2\,SCl = 2HCl + \begin{matrix}S - C_6H_3\begin{cases}OH\\COOH\end{cases}\\|\\S - C_6H_3\begin{cases}COOH\\OH\end{cases}\end{matrix}$$

Salicylic Acid. Dithiosalicylic Acid.

The product of the reaction is a yellow resinous mass. This is dissolved in water containing soda, and the acid reprecipitated by addition of hydrochloric acid.

Physical and Chemical Properties.—Dithiosalicylic acids are described as forming pale yellow powders, soluble in alcohol, while No. II besides being readily taken up by alcohol was said to be very hygroscopic.

Medicinal Uses.—The acids themselves do not seem to have been at all employed in medicine but only the sodium salts.

Sodium Dithiosalicylate No. 1 was the more recently brought under notice as a powerful antiseptic. Added to cultures of the most resistant bacilli in the proportion of 15 per cent. it destroys the life of the microörganisms in from two to fifteen minutes (Hueppe). Employed externally in medicine it proved successful in a severe case of ozæna (Ro-

senbach). Chiefly, however, the substance has found favor in veterinary practice, being applied in 2½ to 5 per cent. solutions (as lotions or compresses) in the treatment of foot and mouth disease. Strikingly beneficial results are reported (Renner, and others), and the substance seems worthy of further trial.

Sodium Dithiosalicylate No. II was first tried in medicine by Lindenborn. It occurs as a greyish-white powder, very hygroscopic and entirely soluble in water. On the addition of acid a precipitate of yellow viscid drops is produced consisting of dithiosalicylic acid. A 20 per cent. solution destroys the spores of anthrax (one of the forms of bacilli most resistant to germicides) in about forty-five minutes (Hueppe), and other experiments showed that the salt is superior in antiseptic activity to salicylate of soda. In rheumatic fever, in gonorrhoic rheumatism and similar cases, it proved an effective remedy (Hueppe, Lindenborn), reducing the febrile temperature, removing pain and bringing about a reduction of local swelling. The dosage adopted was 3 grains twice a day in slight cases, or more frequently when the symptoms were more severe, with intervals of an hour between each dose. Tinnitus and nausea were not observed, and sweating occurred only when more than 12 grains was taken in the course of the day.

Lithium Dithiosalicylate was also prepared for use in rheumatic affections, and gave good results in a few cases of arthritis and gout (Lindenborn, Frank).

DERIVATIVES AND ALLIED COMPOUNDS.

Sulphosalicylic acid, $C_6H_3SO_3H(OH)COOH$, occurs as white crystals, readily soluble in water and in alcohol. It is formed by the action of sulphuric anhydride on salicylic acid.

Salicyl-sulphuric acid, as it is also termed, is a remarkably delicate and precise test for proteids of all classes, albumens, globulins, fibrin, proteoses and peptones. A dense bulky white precipitate is formed, which is not redissolved on boiling unless the body were an albumose or peptone, and then it apears on cooling; the precipitate is readily soluble in dilute alkali. The reagent detects 1 part of white of egg in

12500 parts of water (Mac William). In using it for urine (*ibid* and Roch) the acidity of the latter should be ensured; the tube is shaken quickly and examined at once. The occurrence of an opalescence or cloudiness immediately or within 2 or 3 seconds is an indication of proteids. If the precipitate or opalescence be caused by ordinary albumen or globulin, commonly present in albuminous urine, it does not disappear on heating but on the other hand becomes markedly flocculent. But if due to the presence of albumoses or peptones it clears up on heating (before the boiling point is reached) and appears when the tube cools.

DIURETIN.

Synonym: Sodio-Theobromine Salicylate.

$C_7H_7NaN_4O_2, C_6H_4OHCOONa$.

A definite double compound of sodium theobromine and sodium salicylate.

Preparation.—By the interaction of molecular weights of sodio-theobromine and sodium salicylate in aqueous solution, and evaporation to dryness.

Physical and Chemical Properties.—A white powder, soluble in less than half its weight of water when warmed, the solution remaining perfect on cooling. Theoretically it should contain 49.7 per cent. of theobromine and 38.1 per cent. of salicylic acid.

The preparation is estimated according to the amount of theobromine it contains. The aqueous solution is acidified, then made alkaline with ammonia, and the separated theobromine collected on a filter, washed and dried. By this method a pure compound should yield at least 46.5 per cent. of alkaloid.

Further characteristics of pure diuretin are that it burns away without residue, and dissolves readily and completely in soda solution.

The salicylic acid may be determined by shaking out the acidified filtrate and washings from the theobromine with ether, separating the extract, evaporating off the solvent and weighing the residue. It should not be more than 38.5 per cent.

Caffeine is detected by dissolving the precipitated alkaloid by addition of potash, shaking out the solution with chloroform, and evaporating off the menstruum; residue amounting to more than ½ per cent. of the alkaloid taken is made up to its actual percentage by the more soluble caffeine.

Medicinal Uses.—Like caffeine and theobromine, diuretin has a marked diuretic action; compared with the former it is superior in having no serious or dangerous cardiac action, while it has the advantage over the pure alkaloid of being freely soluble. In doses of from 45 to 90 grains *pro die* in divided portions it acts as a pure diuretic, without effect upon the heart (Gram, Schroeder). Later observers, with a few exceptions, note however that diuretin strengthens and regulates the heart's action, as is shown by an increase of blood pressure and by sphygmographic tracings (Pfeffer, Babcock, Kress, Hoffmann, Geissler). Diuretin has been successfully employed in dropsy of both cardiac and renal origin, in hepatic cirrhosis, and in various diseases of the heart and kidneys accompanied by œdema (above named authors and Pierez). The volume of urine excreted in the twenty-four hours increases during the administration of diuretin three or four-fold, and even more in some cases, without any prolonged after-effect or by-symptoms; exudations of a non-inflammatory character are rapidly absorbed (Masius); slight diarrhœa is not infrequent (Pfeffer, Kress). Given to healthy persons no increase in the quantity of urine has been observed (Hoffmann, Pfeffer).

The daily dose of diuretin is 60 to 105 grains, in divided portions of 15 grains. Being readily soluble in warm water it is best given in the form of mixture, either simply dissolved in water or with the addition of flavoring agents, such as peppermint oil or water, etc. Addition of acid and of acid vegetable juices should be strictly avoided, as they throw out the theobromine, which falls to the bottom of the bottle as a thick

white sediment. It may also be prescribed in pill form, but not well in powders, as it absorbs carbonic acid from the air.

DERIVATIVES AND ALLIED COMPOUNDS.

Lithio-theobromine salicylate, is a compound analogous to diuretin, only differing in the substitution of lithium for sodium. It is a white powder, soluble in 5 parts of water.

According to clinical experiments not yet concluded the substance is a useful diuretic in cardiac dropsy. No unpleasant by-effects could be observed in the use of the double salt. The dose adopted was 15 grains four times a day.

ETHYL BROMIDE.

Synonyms: Brom-ethyl; Ætherbromatus; Monobrom-ethane.

C_2H_5Br.

Preparation.—Alcohol and pure concentrated sulphuric acid are mixed together, allowed to cool, placed in a retort, and powdered bromide of potassium added in small portions, keeping the mixture as cool as possible. When the reaction is complete, distillation is effected at 125° C. on a sand bath. The distillate is purified by washing with potassium carbonate and water, subsequent removal of water by chloride of calcium, admixture of 10 per cent. by weight of fresh almond or olive oil, and redistillation from a water bath.

Physical and Chemical Properties.—A colorless, limpid, inflammable liquid, with a sweet chloroformic odor and a burning taste. It boils, when pure, between 38° and 39° C.; specific gravity 1.38 to 1.39 at 15° C. Not miscible with water, but freely with alcohol, ether, chloroform and oils. Under the combined action of air and light it decomposes, becoming gradually brown and acid in reaction (free bromine and hydrobromic acid).

These impurities are detected by shaking with an equal volume of water, and testing the latter with blue litmus paper and argentic nitrate, when, if hydrobromic acid be present, the former is reddened and the latter precipitated. Traces of free bromine are evidenced by the violet color of

the globules, which reach the bottom of a potassium iodide solution a little more than an inch deep, when a few drops of ethyl bromide are allowed to slowly fall into it. Shaken with an equal volume of pure concentrated sulphuric acid, no coloration should be produced after 24 hours (ethylene and amyl compounds). Of course preparations with the slightest pungent or unpleasant smell are quite unfit for use in medicine.

Medicinal Uses.—Ethyl bromide is very largely used as a general anæsthetic in minor surgery. The narcosis is produced in from ½ to 1 minute, and lasts only a few minutes unless fresh quantities be administered. Its effects are produced more rapidly than those of chloroform, while at the same time it has not the unpleasant after-effects of the latter (Szuman, Nunnely, Lewis, Langgaard and others). An ordinary chloroform mask can be employed, being covered with thick flannel upon which the anæsthetic is poured; the mask is then fitted close to the face. In this way about 3 drachms, seldom so much as 6 drachms, is sufficient to produce the necessary degree of anæsthesia. Its use appears to require caution and watchfulness in consumptives and in patients suffering from cardiac or renal disease. Consciousness is not apparently entirely lost in every case, but the sensation of pain is largely or entirely annulled. The number of narcoses which have been carried out with ethyl bromide is very great; the latest observers (Cockburn-Smith, Ziemacki) report very favorably upon the action of the anæsthetic in several hundreds of cases. It is advised to pour a few drops only to begin with upon the mask, and then about 2 drachms at once, so that it is saturated with the liquid. Recommended in the treatment of children when changing dressings—often a painful operation, and in operating upon goitre (Krecke).

DERIVATIVES AND ALLIED COMPOUNDS.

Ethyl chloride, C_2H_5Cl, is prepared by a patented process involving the direct action of hydrochloric acid upon alcohol under high pressure. It occurs as a colorless liquid, with a pleasant ethereal odor; boiling point 10° C. (50° F.); readily inflammable. The liquid is introduced into commerce in

small tubes, each containing nearly 3 drachms, hermetically sealed with a capillary point. It is employed as a local anæsthetic, acting by the virtue of the intense cold produced by its rapid evaporation. When used the point of the tube is broken off, and the heat of the hand is then sufficient to expel the liquid, through the minute orifice formed, in a stream which can be directed to any desired point. The mucous membrane, *e. g.* of the gum in tooth extraction, is first dried and then rubbed with glycerine or oil; the spray is applied until the membrane becomes white, when the anæsthesia is complete. The tooth itself must be carefully protected from the action of the liquid, and the best results are obtained when the tube is held at some distance from the place to be anæsthesised. During the application the patient should breathe through the nose only (Redard).

The lowest temperature attainable by ethyl chloride is–35° C. Ethyl chloride is recommended for use in minor surgery generally, such as the treatment of ingrowing nail, the opening of abscesses, the relief of facial neuralgia, sciatica, etc., (Ferrand, Grandeclement, Scheller).

The ready inflammability of the compound and its vapor must be kept in mind, and operations performed at a good distance from gas and other flames, or by electric light.

It has the advantage over some other local anæsthetics of being without unpleasant after-effects or influence on the sensorium.

Ethylene bromide, $C_2H_4Br_2$, is a faintly-brown colored liquid, with an odor resembling that of chloroform, and a sweet taste with an after-burning sensation. At 0° C. it solidifies to a snow-white crystalline mass, and its boiling point is 131° C., specific gravity at 21° C. 2.163. Insoluble in water, but miscible in all proportions with rectified spirit, and forming perfectly clear solutions with fatty oils.

In spite of their widely different physical properties, the similarity in name has led to confusion of ethylene bromide and ethyl bromide. It is important to avoid such an error since the ethylene compound is capable of producing marked poisonous effects when inhaled; several such cases are recorded in literature.

As a bromine compound not associated with a powerful basylous radical, ethylene bromide has been used in epilepsy as a substitute for potassium bromide, which, when long continued, produces poisoning symptoms. In 10 cases of epilepsy treated with ethylene bromide the attacks became less frequent, shorter and milder, sometimes degenerating into mere muscular twitchings without unconsciousness (Donath). The dose of the compound adopted was 6 to 12 drops in emulsion, in spirituous solution (equal parts, the dose being stirred up in a glass of milk), or in capsules with ol. amydal. dulc. For subcutaneous injection solutions in oil are recommended.

EUPHORIN.

Synonym : PHENYL-URETHANE.

$C_6H_5NHCOOC_2H_5$.

A crystalline compound structurally allied both to carbaminic acid and to acetanilide.

Preparation.—By the interaction of aniline and chloroformic ethyl ester.

Physical and Chemical Properties.—A white crystalline powder, with a faint aromatic odor, and slight after-taste of cloves. Practically insoluble in water, readily soluble in alcohol, or in mixtures of water and alcohol, such as wines. Melting point 51° C.

Medicinal Uses.—First recommended in 1880 as an antipyretic and antirheumatic, acting as an energetic and safe antifebrile, improving the general well-being, relieving the pain, and reducing the joint swelling in rheumatism without producing collapse and cyanosis (Giacosa, Sansoni, Adler). The analgesic action was also prompt in neuralgias, sciatica, and the like. In a few cases of advanced tuberculosis of the lungs with high evening temperature, the compound was administered with very good success, the temperature falling from 1.4° to 2° C. in half an hour after the administration of the powders (Adler). All the observers speak well of the freedom of the action of euphorin from unpleasant by- or after-effects.

The antiseptic virtues of the preparation have also been made use of in the treatment of ulcers, chronic ophthalmia, skin diseases, and the like. It reduces the secretion of wounds, and the slight amount which persists assumes a serous character. On the other hand, no disturbances of any kind were observed. The most encouraging results were also obtained in general surgery (Oliva). Applied to venereal ulcers deodoration was affected in a few hours, and without the slightest pain the ulcers cleaned up and formed healthy granulations less irritable than those produced by iodoform. Euphorin prevents the spread of the venereal ulcer from the wound to the inguinal glands (Peroni, Bovero).

As an antipyretic the remedy is given in doses of 8 grains, and against rheumatism 6 grains three, four or five times a day, in wafers, dissolved in wine, or suspended in water. Euphorin cannot be prescribed in powders with antipyrine, as a liquid is formed when the two substances are rubbed together (Suchanek). Externally the substance itself is applied as a dusting powder, as ointment (with lanolin), and as superfatted medicinal soap.

EUROPHEN.

Synonym; Di-isobutylortho-cresol iodide.

$$2\left(\begin{matrix}C_4H_9\\CH_3\end{matrix}\right\}C_6H_3O\Big)HI$$

A recent addition to the class of iodoform substitutes, allied to aristol.

Preparation.—By the interaction of isobutyl alcohol and ortho-cresol in the presence of zinc chloride at a high temperature isobutyl-orthocresol is formed. This dissolved in dilute alkali and precipitated with a solution of iodine in potassium iodide, yields the europhen, which is washed and dried in the dark.

Physical and Chemical Properties.—An amorphous yellow powder, of peculiar aromatic odor, reminding somewhat of saffron; insoluble in water and glycerine, readily soluble in alcohol (up to about 30 per cent.), ether, chloroform and fatty oils (up to 25 per cent.); as with aristol the solutions

must be prepared in the cold. In contact with water or aqueous liquid (wound-secretion) small quantities of iodine seem to be given off that are again taken up. Mixed with any fat and starch it is also decomposed, but in ointment form alone is quite stable. It yields iodine to metallic oxides and mercury salts. Europhen is five times as bulky as iodoform. It must be preserved in a dry place and protected from the access of light. Between the fingers it feels resinous, and adheres to the skin and mucous membrane like aristol and much more readily than iodoform.

Europhen, like aristol, may be prepared in a purer condition (free from any trace of iodine which is formed in drying it) by dissolving in alcohol and reprecipitating with water. The product so formed is of paler color and absolutely free from iodine; on the other hand, it is quite inert, having no effect whatever upon the growth and development of bacteria (Goldmann).

When heated Europhen "runs together" at about 70° C., gradually liquefying as the temperature rises, until at about 110° C. it forms a clear brown liquid. The ash amounts to 0.15 per cent.

Medicinal Uses.—Europhen exerts a more or less marked kolyseptic action upon micro-organic growth, probably by virtue of the free iodine which is set free in the nascent state when the compound comes in contact with aqueous liquids. It is undoubtedly equal in this respect to iodoform (Siebel), while the advantages are claimed for it that it is non-poisonous, odorless and specifically lighter. The use of europhen is indicated in all cases where hitherto iodoform has been employed (Eichhoff, Petersen, Loewenstein, Vulpius, Nolda), and it has been applied in nasal diseases, syphilis, ulcus cruris, lupus and burns (Siebel). It is said to have a good effect in syphilis when subcutaneously injected.

For external use europhen is dusted on in powder, or applied as a 5 to 10 per cent. ointment with lanolin. Metallic oxides and mercurials must not be prescribed with it, nor the zinc starch paste, so much used in dermatology. For subcutaneous injection a 3 to 10 per cent. solution in olive oil is applied.

EXALGINE.

Synonym: Methylacetanilide.

$C_6H_5N(CH_3)CH_3CO.$

A crystalline compound allied to acetanilide, first described by A. W. von Hofmann in 1874.

Preparation.—By warming together monomethylaniline and acetyl chloride. The reaction when once started takes place violently, and is represented as under:—

$$2\,C_6H_5NHCH_3 + CH_3COCl = C_6H_5N(CH_3)CH_3CO +$$

Monomethylaniline Acetyl chloride

$$C_6H_5NHCH_3\,HCl.$$

Monomethylaniline hydrochloride.

The monomethylacetanilide is obtained by dissolving the mass in boiling water and crystallizing out. The unchanged methylaniline is recovered by distillation from excess of soda.

Physical and Chemical Properties.—Exalgine occurs in beautiful acicular needles, difficultly soluble in cold, more readily in warm water, more easily so in dilute and concentrated alcohol. It melts at 100° C., and boils between 240° to 250° C. without decomposition.

It is converted by soda incompletely, and more readily by concentrated hydrochloric acid, into monomethylaniline. Aniline and other compounds of the base are detected, if present, by the production of a violet color when solution of chlorinated lime is added to the solution of monomethylaniline in hydrochloric acid after it has been nearly neutralized by ammonia.

Acetanilide and aniline salts are also detected by the odor of isonitril produced when the impure exalgine is heated with alcoholic potash and chloroform. By the provision that the aqueous solution shall not be changed by silver nitrate the absence of hydrochloric acid is ensured.

Exalgine is distinguished from acetanilide, methacetine and phenacetine by treating 2 grains with 20 minims of concentrated hydrochloric acid: insoluble = phenacetine. Acetanilide dissolves, but separates again in crystals. Methacetine also dissolves, but the solution is gradually colored reddish-brown on the addition of one drop of concentrated nitric acid.

Something has been written as to the possible confusion of exalgine and strychnine, but there seems to be no more danger in this direction with exalgine than with the number of other organic compounds which crystallize in the same form.

Medicinal Uses.—Exalgine was introduced in the expectation that it would take a foremost place in materia medica as an analgesic. Experiments on animals, however, showed it to have a powerful poisonous action, a d as it was employed in medical practice a series of cases were reported in which its use, especially in overdoses by error, was followed by toxic effects resembling those of carbolic acid, with delirium, dyspnœa, cyanosis, and renal disturbances (Buisson, Dyer, and Prentiss most recently). On the other hand, some observers record excellent results in neuralgias, characterize the remedy as superior to antipyrine, and without serious by-effects (Dujardin-Beaumetz, Bardet, Gardineau). Antithermic effects are not produced unless poisonous quantities be given (Fraser). Given with success in chorea in daily doses of 3 grains (Moncorvo). Its name (from ἐξ, and ἄλγος, pain) was given to indicate its chief field of usefulness.

There has been a good deal of difference of opinion as to the dose of exalgine, but the balance undoubtedly lies in favor of comparatively small doses, ½ to 4 grains, not exceeding 5 grains. Sometimes prescribed in powder, occasionally in pills, but most frequently in mixtures with some form of alcohol; half a drachm of rectified spirit and one ounce of water form a permanent solution with 16 grains. Useful formulæ are:

I.	II.
℞ Exalgini.....gr. 48	℞ Exalgini.....gr. ii
Tr. cort. aur..... ʒ iss	Sp. vini gall..... ʒ ss
Syr. aurant..... ... ʒ i	Syr. aurant..... ʒ iii
Aquæ.....ad ʒ vi	Aquæ.....ad ʒ ii
M. Each tablespoonful contains 4 grains.	M.

It is recommended in dispensing, to dissolve the exalgine in slightly warm, not hot, water and add the spirit and flavoring; so made the solutions are permanent.

GALLACETOPHENONE.

$CH_3COC_6H_2(OH)_3$.

A derivative of pyrogallol containing an acetyl group as well as three hydroxyl groups. Introduced primarily under the less intelligible name "Gallacotophenone."

Physical and Chemical Properties.—A pale yellow powder, crystallizing from hot water, in which, as also in alcohol and in ether, it is readily soluble. Cold water takes up only 1.8 per mille, but by the addition of 30 per cent. of sodium acetate a 4 per cent. aqueous solution can be made; glycerine dissolves it in every proportion.

Medicinal Uses.—Recommended instead of pyrogallol, which often gives rise to poisoning symptoms, in the treatment of psoriasis; gallacetophenone has less powerful reducing properties than pyrogallol, and the further advantage that it does not soil the linen with which it comes in contact.

Gallacetophenone having been proved harmless to animals was tried in a few cases of psoriasis in human beings with encouraging results. A good effect is observable within 12 hours after the application (Rekowski).

GUAIACOL.

Synonym: METHYLPYROCATECHIN.

$C_6H_4OHOCH_3$

A liquid compound constituting from 60 to 90 per cent. of creasote.

Preparation.—By fractional distillation of beechwood-tar creasote, the fraction passing over between 200° and 205° C. being collected. This is freed from acid compounds by agitation with ammonia, and fractionated again. The lower boiling fraction is dissolved in an equal volume of ether, and decomposed with a concentrated alcoholic solution of potash, potassium-guaiacol being formed. This is washed with ether, crystallized from alcohol, and the guaiacol set free by dilute sulphuric acid. Another method involves precipitation of

creasote with barium hydrate ($BaHo_2$), and separation of the compounds formed, advantage being taken of their differing degrees of solubility.

The preparation of absolutely pure guaiacol—even the "guaiacol absolut." of commerce contains foreign compounds, such as cresols—is effected from repeatedly recrystallising benzoyl-guaiacol, which is odorless and with a constant melting point of 45° C. This is saponified by boiling with the quantity of alcoholic potash calculated to take up the amount of benzoic acid combined with it under a return condenser. After evaporation of the alcohol, shaking out with ether and volatilizing off the solvent, the guaiacol is obtained and is further purified from small quantities of ethyl benzoate by solution in dilute soda, filtering, setting free by sulphuric acid, washing, drying and rectifying.

Physical and Chemical Properties.—The chemically-pure monomethylpyrocatechin, obtained by the second process described above, is a somewhat colored liquid, with an agreeable odor, a sp. gr. at 15°C. of 1.133, and boiling at 206° to 207°. Soluble in water in the proportion of 1 to 85, in petroleum benzin 1 to 8 (Bongartz). Readily soluble in alcohol and ether.

With concentrated sulphuric acid it gives a faint yellow coloration, which is changed to cherry red by the addition of a small proportion of acetone. In alcoholic solution it gives a blue color with a trace of ferric chloride, changing to green as more of the salt is added. This reaction is characteristic.

The various guaiacols of commerce differ from the above characters in having a lower specific gravity and boiling point, and in giving more or less red color with concentrated sulphuric acid alone. They darken on exposure to air and light. Guaiacol is excreted with the urine, and also makes its appearance in the saliva and perspiration. The method of detecting it is described under **Benzosol** (*q. v.*).

The compound forms crystalline salts with the metals, an atom of these elements displacing the hydrogen of the hydroxyl group, as potassium guaiacol: $C_6H_4OCH_3OK$. The compounds are, however, unstable and decomposed by much water. It also combines to definite chemical bodies with

acid radicals; some of these, which have been introduced into medicine, are described below.

Medicinal Uses.—According to Guttmann, tubercle bacilli are destroyed by blood which contains ½ per mille of creasote, while even half that proportion arrests their growth. On this statement the intensive creasote treatment of phthisis was based, which consists in commencing with a daily dose of 2 minims and increasing the amount 1 minim daily, until 15 to 18 minims are being taken *pro die* in the form of capsules; in this way an accumulation of creasote in the blood and fluids of the tissues has been believed to be attained corresponding to that pointed out by Guttmann as theoretically necessary (Sommerbrodt, Schetelig). Guaiacol was introduced as a substitute for creasote, being the principal ingredient of the latter and of definite chemical nature; the same dosage as that given above for creasote has frequently produced distinctly beneficial effects in the early stages of the disease.

It is interesting to note that quite recent researches indidate that the good effects of the creasote or guaiacol treatment of pulmonary tuberculosis are due neither to the kolyseptic (or development-hindering) properties of guaiacol, as some authors (including the originator of the treatment) believe, nor purely to its stomachic and tonic virtues (as others have asserted), but to the fact that it forms compounds, eliminable from the blood in a dissolved state with the toxic albuminous by-products of the activity of the tubercle bacillus (Hoelscher and Seifert). It is to these albumenoids that the fever, night sweats, and disturbances of appetite, digestion and general well-being must be ascribed, and with their removal or conversion into inert compounds all these symptoms disappear, as seen in the action of guaiacol and the various compounds described below.

Guaiacol is administered in mixture with wine or brandy (best after meals), or in capsules, or combined with cod-liver oil. Also employed in the form of inhalations, 5 to 10 drops with hot water being inhaled several times a day (Schueller). Subcutaneously 3 to 15 minims have been injected in the pure state (Schetelig, Polyak, Bourget), or in 20 to 30 per cent. solution in almond oil.

Finally guaiacol has done good service in the disinfection of tooth pulp instead of creasote (Gorgas).

DERIVATIVES AND ALLIED COMPOUNDS.

Guaiacol carbonate.—Under this name a substance was described in 1890 as possessing antiseptic and antipyretic properties. It was obtained, according to a patented process, by saturating sodium-guaiacol with carbon dioxide, heating the mixture in closed vessels to 100° C., and separating the acid from the product by treatment with a mineral acid. The product melted at 148° to 150° C. and also was said to serve for the preparation of azo-dyes.

Towards the end of 1891 another derivative was brought under notice which was also called guaiacol carbonate, but from the formula $CO(OC_6H_4OCH_3)_2$ seems to be more of the nature of a ketone. This compound forms neutral crystals, free from taste and odor, and insoluble in water; melting point 86° to 90° C.

Like benzosol this compound is to be used as a substitute for guaiacol and creasote in the treatment of tuberculosis. In doses of 6 to 8 grains, gradually increasing to 1½ drachms *pro die*, it produces improvement of appetite and increase of nutrition, and consequently of body-weight and of resistance to the effects of the disease (Hoelscher). The preparation is well borne, as it does not irritate the mucous membrane or disturb the digestive functions.

Guaiacol biiodide is a compound made by acting upon crystalline sodium guaiacol dissolved in water with an aqueous solution of iodine and iodide of potassium. A reddish-brown precipitate is formed which, when collected, washed and dried, has an odor reminding of iodine; it melts on the water-bath, is soluble in alcohol and fatty oils, and readily decomposable. Guaiacol biiodide is believed by its discoverer (Vicario) to be suitable for application as a remedy in tuberculosis.

Styracol is described as the cinnamic acid ester of guaiacol, or cinnamyl-guaiacol, represented by the formula $C_6H_5.CH:CH.CO_2C_6H_4OCH_3$. It is prepared by the interaction of equal

molcules of guaiacol and cinnamyl chloride, the mixture being heated for a short time on a water bath, after two hours standing. The resultant mass is treated with boiling alcohol, the solution filtered and allowed to cool; long needles are deposited, which are purified by re-crystallisation. The pure product melts at 140° C. Styracol is said to be a strong antiseptic, useful when administered internally in chronic vesical catarrh, gonorrhœa, and catarrhal affections of the digestive tract. It was also introduced as a substitute for guaiacol in the treatment of phthisis.

HYDRACETINE.

Synonyms: Pyrodine; Acetylphenylhydrazine.

$C_6H_5\ HN\text{-}NHCH_3CO.$

A crystalline compound, which may be regarded as hydrazine (*v.* Hydroxylamine), $H_2N\text{-}NH_2$, in which hydrogen atoms are replaced by the monivalent groups phenyl and acetyl.

Preparation.—By heating together phenylhydrazine and acetic anhydride, dissolving the product in boiling water and crystallizing.

$$2\,C_6H_5N\text{-}NH_2 + (CH_3CO)_2O = 2\,C_6H_5HN\text{-}NH\ CH_3CO + H_2O$$

Phenylhydrazine. Acetic anhydride.

Also by the prolonged action of glacial acetic acid on phenylhydrazine, distilling off excess of acid and crystallizing.

The name "Pyrodine" appeared first in literature under the authority of Dr. Dreschfeld in England at the end of 1888, but a few weeks subsequent to the first paper, the above named author explained that pyrodine was an impure acetylphenylhydrazine.

Physical and Chemical Properties.—Colorless hexagonal lustrous prisms, odorless and practically tasteless; melting point 128° to 129° C. Soluble in 50 parts of water at 15° C. and in 8 to 10 parts of the same solvent at 100° C.

Boiled with concentrated hydrochloric acid it splits up into acetic acid and hydrochlorate of phenylhydrazine. Like methacetine and phenacetine it forms a colorless solution with sulphuric acid, which is turned red by nitric acid. Added to

a solution of silver nitrate, lustrous metallic silver is thrown down, and similarly it precipitates gold from auric chloride, flecks of metal appearing on the surface of the liquid.

The absence of acetic acid is shown by the neutrality of solutions. Boiled a few minutes with 30 parts of concentrated hydrochloric acid it dissolves; if chlorinated lime solution is added to the cold liquid diluted with 100 parts of water, a yellow tint is produced (violet indicates acetanilide).

Medicinal Uses.—Like the allied body phenylhydrazine, and like hydrazine itself, this compound is a well-marked blood-poison exerting a solvent action upon the corpuscles so as to be capable of producing anæmia; for this reason care has to be taken in its use, both internally and externally, the effect being cumulative, and manifested in malaise, weakness, and a kind of angina.

The substance was first recommended as an antipyretic (Dreschfeld, Guttmann) internally in doses of ⅙ to 1 grain, not exceeding 2 grains daily and then not more than three days consecutively. Externally in 10 per cent. ointment it has been employed against psoriasis instead of chrysarobin. In both these directions, however, the use of hydracetine seems to have greatly fallen off, and no additions have been made to its literature for a considerable time.

HYDROXYLAMINE HYDROCHLORIDE.

$NH_2OH\,HCl$.

A crystalline salt of a base analogous to ammonia, and known in the free state only in solution.

Preparation.—By the interaction at 0° C. of sodium hydrogen sulphite in concentrated solution and sodium nitrite. The readily soluble sodium salt is by the addition of potassium chloride converted into the difficultly soluble potassium hydroxylaminedisulphonate. By the action of heat upon solution of the latter it is split up into hydroxylamine sulphate and potassium sulphate which are separated by fractional crystallization, and from the former the hydrochloride is obtained by decomposition with barium chloride.

The two reactions may be represented as follow:—

$$NaNO_2 + 2NaHSO_3 = HO.N(SO_3Na)_2 + NaOH.$$

Sodium hydroxylaminedisulphonate.

$$2HO.N(SO_3K)_2 + 4H_2O = (NH_2OH)_2H_2SO_4 + 2K_2SO_4 + H_2SO_4.$$

Hydroxylamine Sulphate.

Physical and Chemical Properties.—Colorless hygroscopic crystals similar in form to ammonium chloride. Soluble in an equal weight of water, also in glycerine and in 15 parts of alcohol. The solutions redden blue litmus, but do not affect congo-paper provided hydrochloric acid be absent.

Chemically the compound is distinguished by an enormous reducing power, precipitating metallic gold, silver and mercury from solutions of their salts, and throwing down cuprous oxide from Fehling's solution in the cold. The hydroxylamine itself is oxidized thereby to nitrous or nitric oxide and nitrogen acids.

Iron is detected by potassium ferricyanide or thiocyanide; barium by sulphuric acid; and fixed impurities generally by ignition, when no residue should be left. It is distinguished from sal ammoniac by forming a clear solution with 20 parts of absolute alcohol.

Hydrochloric acid is volumetrically estimated by normal potash, using phenolphtalein as an indicator, and hydroxylamine, by excess of decinormal iodine solution, decomposing the excess with sodium thiosulphate and titrating back with $\frac{n}{10}$ iodine, using starch as an indicator.

$$2NH_2OH\,HCl + 4I = N_2O + 3HCl + 4HI + H_2O.$$

Hydroxylamine hydrochloride must be kept in well closed bottles.

Medicinal Uses.—Hydroxylamine hydrochlorate was suggested as a non-staining substitute for the reducing bodies pyrogallol, chrysarobin and anthrarobin in the treatment of skin diseases. It proved effective in lupus (Eichhoff, Fabry), in mycosis tonsurans, sycosis parasitaria, psoriasis, etc. (Burz). Some authors pronounced it to be dangerous if absorbed (Groddeck), and, like the amine compound previous-

ly mentioned, it is a powerful poison to the blood and generally antagonistic to vegetable and animal life.

DERIVATIVES AND ALLIED COMPOUNDS.

Hydrazine, or *Diamine*, N_2H_4, is a somewhat allied and similarly reducing body. It is also a general poison to animal and vegetable life; germinating cotyledonous plants and algæ, infusoria, crustaceans, and insect larvae, young snakes and rabbits being alike killed by it (Loew and Buchner). Peptone solutions containing 1 per mille of diamine sulphate are no longer able to support bacterial life, and the solutions remain unchanged for weeks. Diamine also kills the germs of mould.

HYPNONE.

Synonyms: ACETOPHENONE; METHYLPHENYLKETONE.

$C_6H_5\,CO\,CH_3$.

A liquid compound long known to the chemist and classified among mixed ketones.

Preparation.—By the dry distillation of calcium acetate and calcium benzoate. The crude product (containing about 6 per cent. of hypnone) is purified (from toluol, diphenyl ketone and cumarin) by repeated fractional distillation, solidified by cold, the adhering liquid removed by bibulous paper and again rectified. The reaction by which methylphenylketone is formed is probably

$$\left.\begin{matrix}CH_3COO\\CH_3COO\end{matrix}\right\}Ca + \left.\begin{matrix}C_6H_5COO\\C_6H_5COO\end{matrix}\right\}Ca = 2CaCO_3 + 2\left\{\begin{matrix}CH_3\\C_6H_5\end{matrix}\right\rangle CO.$$

Calcium acetate. Calcium benzoate. Hypnone.

Physical and Chemical Properties.—When pure, hypnone is a colorless oily liquid, with a peculiar odor and a pungent taste. Specific gravity, 1.032; at 14° C. it solidifies, melting again at 20°.5 C. (Staedel and Kleinschmidt). Very little soluble in water, but readily miscible with alcohol, ether and fatty oils.

Chemically, hypnone has all the properties of a true ketone, but does not form a crystalline compound with sodium hydrogen sulphite. Free acids must not be present, therefore it should not alter blue litmus paper, and the

absence of benzaldehyde and cumarin is required by providing that one drop of hypnone in 3 drachms of $\frac{n}{1000}$ permanganate must not decolorize the latter within two minutes.

Medicinal Uses.—First recommended as a hypnotic in 1885 (Dujardin-Beaumetz), being regarded as superior to chloral hydrate and to paraldehyde. Did not prove very successful in the treatment of mental diseases (Rottenbiller), while also patients soon become habituated to its effects so that the doses had to be continually increased (Seifert). Hypnone reduces blood pressure and slows the respiration, so that care must be exercised in its administration (Grosset). The dose is 1 to 3 minims.

ICHTHYOL.

Synonym. Ammonium Ichthyol Sulphonate.

$C_{22}H_{36}S_3O_6(NH_4)_2$.

The most important of the salts of ichthyolsulphonic acid, prepared from a bituminous mineral of Tyrol, which is rich in fossilized remains of fish and sea animals, whence the name "ichthyol" (*ἰχθύς* fish).

Preparation.—By dry distillation of the bituminous mineral, there passes over, between 100° C. and 225° C., a crude volatile oil. This is treated at 100° C. with an excess of concentrated sulphuric acid, and the resultant ichthyolsulphonic acid precipitated several times by concentrated brine to obtain it free from excess of acid.

Physical and Chemical Properties.—The product of the process outlined above contains a certain proportion of unchanged volatile oil, which gives it a peculiar odor. This oil cannot be removed without bringing about decomposition.

Ichthyol contains a high proportion of sulphur—about 10 per cent. (Baumann and Schotten)—combined in a manner not well understood; it cannot be extracted by boiling with aqueous or alcoholic potash, nor by treatment with sodium amalgam. When warmed with methyl iodide no crystalline compound is formed, such as the sulphides of the fatty series are known to yield.

The product of the saturation of the ichthyolsulphonic acid with ammonia is a clear reddish-brown viscid liquid, with a bituminous odor and taste. It is miscible with water (the mixtures being faintly acid); alcohol and ether dissolve it in part; petroleum benzin takes up very little. From aqueous solutions hydrochloric acid throws down a dark resinous mass, soluble in ether and in water (but not in dilute acids or solution of sodium chloride). The action of potash developes the odor of ammonia, and the mixture dried and carbonized forms a mass which gives off sulphuretted hydrogen when treated with hydrochloric acid. Dried in a water-bath, ichthyol loses about 45 per cent. of its weight.

Medicinal Properties and Uses.—The application of ichthyol in medicine, according to the very large experience hitherto obtained, depends chiefly upon three factors: (1) its reducing property, (2) its antiseptic action, (3) its vascular contractile effect. From this combination of properties, ichthyol has proved useful as an antiphlogistic, an alterative, anodyne, resolvent, gastric and renal tonic, and astringent. That the substance has a true kolyseptic power, *i.e.*, exerts a restraining influence upon the development of bacteria, has been proved bacteriologically (Fessler, Klein), and confirmed repeatedly by practical experience; its peculiar virtues are largely ascribed to the high proportion of sulphur it contains.

The usefulness of the remedy was first brought under the notice of the medical profession in 1883, it being recommended in skin diseases merely (Unna). Since then, as already indicated, the list of affections in which it has been successfully employed has grown to such a length that by some authors the substance has been looked at askance as a "panacea" or "cure-all." It appears, however, that many, perhaps most, of the diseases for which ichthyol has been recommended are caused by or associated with anomalies of circulation and capillary dilatation on which its vascular contractile property has a specific action (Nussbaum, Schweninger). Internally it retards the disintegration of albumens and favors their formation and accumulation (Zuelzer, Charles).

The literature of ichthyol is of very large dimensions, rendering it impossible to deal with it all. The more recent

additions are confirmatory of those previously made, and present a few new features of the remedy. It has a remarkable effect—especially when applied externally and given internally simultaneously—upon exudations, not only in gynæcology (Freund, Reitmann, Schoenauer, Kotschau, Kurz, Albertoletti, Bergesio) but also in such affections as pleurisy (A. Mueller); pain is promptly alleviated—this anodyne action is one of the most valuable properties of ichthyol for gynæcological diseases (Lehmann)—and the exudation is gradually reabsorbed.

Even in very dilute solutions ichthyol arrests the development of the bacilli of erysipelas and pus (Fessler, Klein), and practically it has done excellent service in erysipelas (Rosenberg). The surrounding parts being carefully washed, pure ichthyol, the collodion or ointment, is spread over them and the affected area; fever subsides, and the course of the disease is shortened and its severity moderated.

In ulcers of the leg, painting with pure ichthyol is effective (Hartmann); the painted part is covered with cotton wool, unstarched bandage and the stocking. Renewal is necessary every three or four days. Eczema and a long list of skin diseases are beneficially influenced by the ichthyol treatment (Bulkley, McLean, Cranstoun Charles, Iliinsky), and for chilblains it has been pronounced unfailing—a 30 per cent. ointment relieving irritation at once and completely (Macpherson). For rheumatism ichthyol is indispensable (Iliinsky); a 50 per cent. ointment is applied locally and the remedy itself given internally. Its use in surgery generally should also be mentioned.

Internally the remedy has been given and recommended for various affections of the digestive and intestinal tract (Jawitzky), of the kidneys, in syphilis (Peroni), leprosy, etc. Many more authorities might be mentioned, but only those reports of recent date have been specially referred to. During the influenza epidemics attention was called to the value of inhalations of ichthyol (Lorenz).

Ichthyol is prescribed for external use pure, in ointment form with lanolin (10 to 50 per cent.), as liniment with turpentine or an equal weight of a mixture of lanolin and olive

oil (with 30 per cent. of chloroform in rheumatism), as soap, etc. In gynæcology it is much used in combination with glycerine (1 of ichthyol in 10), and against erysipelas as a 10 to 25 per cent. collodion (ichthyol and ether, of each 5 parts, collodium 10 parts) with or without the addition of castor oil. A solution in eight parts of a mixture of absolute alcohol and ether, or of chloroform and spirit of camphor (1:4), is employed in neuralgia. The odor of the remedy in these preparations may be disguised by the addition of cumarin, vanillin, or citronella.

Internally ichthyol is given—dose 5 to 20 minims—in milk, cocoa or beer, or in pills (the sodium salt being prescribed). Suppositories are made up with cacao butter, as also pessaries; for the latter purpose capsules containing the 10 per cent. ichthyol glycerine have been used.

DERIVATIVES AND ALLIED COMPOUNDS.

Other salts of ichthyol sulphonic acid are the ichthyolsulphonates of sodium, lithium, zinc and mercury. They all occur as brownish, black, tar-like masses, but the first is the only one of any importance. Being solid it is employed when it is desired to give ichthyol in pill form.

IODOL.

Synonym: TETRAIODOPYRROL.

C_4I_4NH.

A crystalline compound first prepared in 1885 by Ciamician and Silber.

Preparation.—By the interaction during 24 hours of iodine and pyrrol in alcoholic solutions. The mixture is then diluted with water, when the iodol separates in crystalline yellow flocks,

$$\underset{\text{Pyrrol.}}{C_4H_4NH} + 8I = 4HI + \underset{\text{Iodol.}}{C_4I_4NH};$$

or the formation of hydriodic acid may be avoided by using aqueous solutions of pyrrol with soda or potash, and of iodine with potassium or sodium iodide, collecting the precipitate, dissolving in alcohol, decolorizing with animal

charcoal and reprecipitating. There are also other methods involving the use of metallic oxides for the same purpose.

Physical and Chemical Properties.—Pure iodol is a pale yellow, more or less crystalline, bulky powder, free from odor and taste. It is practically insoluble in water, and slightly soluble in diluted alcohol. Strong alcohol takes up a third of its weight, which is precipitated from solution by water but not by glycerine. Ether dissolves its own weight of iodol, and fatty oils about one-fifteenth.

When heated gradually iodol is unaffected up to 100° to 120° C., but between 140° and 150° C. it is decomposed with the evolution of violet iodine vapors; if the heat is maintained it finally burns away without residue.

Metals, if present, are detected by sulphuretted hydrogen, and iodides by argentic nitrate.

Medicinal Uses.—Iodol was introduced as an iodoform substitute, having the advantages of being odorless and non-toxic. Has been specially recommended for the treatment of syphilitic ulcers (Mazzoni, Szadek), but also for use in general surgery and inflammatory conditions (Wolff, Schmidt, Markus, Pick). A specially prepared crystalline form has been recommended for application to the mucous membrane as not "balling" like the ordinary powder; insufflation of this crystalline iodol has proved useful in ozæna, and it has also been successfully employed in caries of bone, tuberculous ulcers, diseases of the tonsils, trachea and larynx (Schaffer).

Internally—in doses of 8 to 15 grains, two to four times a day, in wafers—iodol has been recommended when the long-continued but not too powerful effects of iodine are indicated (Szadek).

Like iodoform, iodol is used as a dusting powder, in alcoholic or ethereal solution, with ether and collodium (iodol 1, ether 5, collodium 50); a 5 to 10 per cent. ointment is also applied. In gynæcology tampons are employed soaked in a solution of iodol, spirit and glycerine (1 : 16 : 34). The same solution, or a 10 to 20 per cent. ethereal solution, has been used for injection into fistulæ and abscess cavities. Iodol is believed to stimulate granulation.

DERIVATIVES AND ALLIED COMPOUNDS.

Thiophen, C_4H_4S. This body, closely allied to pyrrol and furfuran in constitution, was discovered in coal tar benzene by Victor Meyer in 1883. It forms a colorless, mobile, oily liquid, with a feeble odor, boiling at 84° C., and not miscible with water.

The compound itself has not been employed in medicine, but two derivatives have,—namely, sodium thiophensulphonate (C_4H_3S-Na SO_3) and thiophen diiodide ($C_4H_2I_2S$). The former is a white crystalline powder, and contains 33 per cent. of sulphur. The diiodide crystallizes in beautiful tables; it is insoluble in water, but taken up abundantly by the other usual solvents. Thiophen diiodide melts at 40.5° C., and is volatile at ordinary temperatures; it contains 9.5 per cent. of sulphur.

The sodium salt was used with good success in prurigo (Spiegler), proving superior to β-naphtol, non-poisonous and non-irritating; it can be used where β-naphtol is contra-indicated.

The diiodide was employed externally as gauze and as powder in a number of cases where iodoform is the usual application, such as mammary carcinoma, phlegmonata, mastitis, caries, bursitis, and certain surgical cases. Symptoms of poisoning were never observed, nor did eczema form. On the other hand, secretion dried up, deodoration was perfect, and granulations firmer than those which developed under iodoform (Hock).

LANOLIN.

Synonym: Adeps Lanæ Hydrosus.

The purified cholesterin fat of sheep's wool containing not more than 30 per cent. of water.

Preparation.—From crude wool fat by emulsification with hydrate or carbonate of the alkalies, and "separation" (into a kind of cream and whey) in centrifugal machines. From the "separated" cream the cholesterin fats are set free by addition of solution of calcium chloride, and the impure lanolin thus obtained purified by repeated melting and wash-

ing, and finally by extraction with acetone, which does not dissolve the contaminating calcium soap.

Physical and Chemical Properties.—A whitish, unctuous substance, free from odor. It does not affect moist litmus. Insoluble in water, only partly soluble in alcohol, but readily so in ether, benzene (benzol) and acetone.

Kneaded with water for some time, lanolin should take up about 100 per cent. of water without slipping smoothly off a spatula ; preparations containing soap exhibit this absence of adhesiveness.

With respect to the proportion of water present, the B. P. Add. requires that 100 grains heated on a water bath till of constant weight shall yield not less than 70 grains. It is further characteristic of a pure preparation that the supernatant layer of fat obtained when the substance is heated with five times its weight of water in a water bath is a clear pale yellow oil.

This supernatant fat (*Adeps Lanæ* B. P. Add.) should be separated from the aqueous liquid and especially examined. According to the B. P. Add. [2nd Ed.] it should have a melting point between 37.8° C. and 44.4° C. (the former figure is certainly too low, as under 40° C. there is hardly any evidence of melting in anhydrous lanolin), and 10 grains should dissolve almost completely in 14 fluid drachms of boiling alcohol, the greater part separating in flocks on cooling. (The intention here is presumably to distinguish lanolin from glycerine fat.) Ignited with free access of air it must also leave but a trace of ash (0.1 per cent. of inorganic salts); and 50 grains dissolved in 4 fluid drachms of ether, with 2 drops of phenolphtaleïn tincture should not require more than 2 grain measures of volumetric soda solution to produce a permanent red coloration. (This test restricts the allowable amount of free fatty acids present to a trace.) "Heated with solution of soda no ammoniacal odor should be evolved," so that ammonia compounds must not be present.

Of the identity tests for cholesterin that of Salkowsky is adopted, involving the production of a purple red color when a chloroformic solution is gently poured over sul-

phuric acid. If the operation be carefully performed the surfaces of contact show a fiery brownish-red zone, which recalls the color of bromine, while the supernatant layer of chloroform immediately above has a violet tint and the upper portions remain colorless.

Liebermann's test, which involves the production of a color not given by glycerine fats, consists in dissolving about two grains of lanolin in about 1 fluid drachm of acetic anhydride, and dropping concentrated sulphuric acid into the solution; a rose-red color is produced, which rapidly changes to green or blue.

Another character which distinguishes lanolin from glycerine fats is that it cannot be saponified by the action of aqueous alkalies. The saponification of lanolin—*i.e.*, the separation of the fatty acids from the cholesterin—is only effected by heating the substance with alcoholic potash or by melting with the solid hydrate. The peculiar stability of lanolin (its non-liability to rancidity) must be ascribed to this firm combination between the cholesterin and the fat acids.

Medicinal Uses.—The fat peculiar to wool and keratin tissues generally was used in medicine centuries ago, but in a very impure condition, under the name "oesypus." This malodorous and irritating substance fell out of use and was altogether forgotten until the introduction of the purified cholesterin-fat by Prof. Liebreich, who made an intimate study of the properties of lanolin. Three factors have been of great weight in determining the permanent retention of the substance in materia medica, as an application to the skin and as a vehicle for the external employment of medicaments of all kinds; these are (1) its great stability, *i.e.*, its resistance to the agents that induce rancidity; (2) its property of taking up a large quantity of water without losing its ointment-like consistence, and (3) the readiness and completeness with which it is absorbed by the skin. To these must be added, as no less important, that lanolin is perfectly free from any irritating constituents.

When lanolin is rubbed upon the skin it is rapidly taken up by the membrane—to which in a sense it naturally apper-

tains—any medicaments mixed with it being at the same time absorbed (Liebreich, W. G. Smith, Paulowsky, Vogel, Bernatzek, Wende, Shoemaker, and others). Its use is therefore indicated in all cases where it is desired to saturate the skin with fat, as for instance in a certain class of skin diseases, or to affect the deeper tissues as in the inunction treatment of syphilis. Experiments on the length of time after which medicaments (*e.g.*, iodine preparations) applied with lanolin to the skin can be detected in the urine, have established the unequalled rapidity with which the substance is absorbed. At the same time this energetic absorption makes perfect purity the more essential. The irritating foreign ingredients (*e.g.*, fatty acids of an impure preparation) would be applied under circumstances the most favorable to the production of a maximum irritant effect.

In consequence of the readiness with which lanolin absorbs water and aqueous liquids, it adheres well to the mucous membrane—a great advantage, of course, in the medication of that tissue. It reduces irritation, and can be employed in gonorrhœa as ointment, bougies, or injection.

Searching experiment has proved that lanolin resists the decomposing action of micro-organisms ; it contains nothing which these forms of life can split up and feed upon, and hence a thin layer is a perfect barrier to their progress, while, further, the base itself is always free from germs (Fraenkel, Gottstein).

The advantages of lanolin over other ointment bases are so marked that it has been almost exclusively and universally adopted for the application of the newer remedies in ointment form. Even acids, acetate of aluminium, chloride of calcium, hydrogen peroxide, sulphurous acid, and other substances of which hitherto ointments could not be usefully prepared, may be successfully applied with lanolin (Unna). The sole practical objection to the use of lanolin for ointments containing only solid ingredients is its stickiness, and this is readily overcome by mixing it, as the writer has previously recommended, with liquid paraffin and ceresin, or with one-third of its weight of vaselin, (*i.e.*, petrolatum). This diluted lanolin or unguentum lanolini, as it was named by

the deviser, meets all the requirements of a good ointment base, and its value has been confirmed by the experience of numerous medical authorities. It is the most suitable form in which lanolin can be prescribed (Paschkis).

Unguentum lanolini with 60 per cent. of water has been warmly recommended as an extraordinarily active remedy for the relief of itching. The evaporation of the suspended water cools the epidermal surface and reduces capillary hyperæmia; the ointment is especially valuable in the treatment of measles, scarlet fever, chicken-pox, etc. (Klein). The preparation has not the sometimes unpleasant adhesiveness of the unmixed lanolin, while it has all the useful therapeutical properties of the latter. Any application in solid or liquid form can be readily mixed with it, and the ointment so made will keep good and free from rancidity for an indefinite length of time. The writer has samples of mercurial ointments made with lanolin ointment which have kept unchanged for two years.

The resistance of lanolin to chemical agents which tend to decompose most organic substances lead to its use for the purely pharmaceutical purpose of massing permanganate of potassium and some other refractory substances for pills.

As a cosmetic, lanolin plays an important part, each of its distinctive properties being of special significance in this application. Cold creams, pomades, milks, emulsions, soaps, etc., are made with it, of which some of the many formulæ may be given as examples. Lanolin-pomade can be prepared from 85 parts of the anhydrous basis and 25 parts of coco-nut oil; lanolin-milk is an emulsion of 10 parts of lanolin, 1 part of borax and 100 parts of rose water. For injection into the urethra a mixture is made of anhydrous lanolin 25 parts, almond oil 75 parts, with the addition of zinc sulphate ½ part (dissolved in 4½ parts of water) or of salicylic acid ¼ part, or of resorcin 1½ parts. Lanolin (anhyd.) and soft soap, in the proportions of 4:5 respectively, form sapolanolin, by means of which mercurials and other remedies are applied to the skin. Another preparation used as a basis in dermatology is anhydrous lanolin 4 parts, wax 4 parts and olive oil 2 parts; 1 part of lanolin (anhyd.) with

2 of benzoated lard and 3 or 6 of water form excellent bases for cooling ointments or creams (Unna). In the manufacture of the so-called "superfatted soaps" a good many manufacturers now use lanolin as the most suitable form of adding the excess of fat. From 5 to 10 per cent. of lanolin is added to the soap mass with or without the addition of a small proportion of olive oil.

DERIVATIVES AND ALLIED COMPOUNDS.

Thilanin, or brown, sulphurated lanolin, is a preparation prepared by the action of sulphur upon lanolin; the product, which contains 3 per cent. of the active ingredient, is an ointment-like mass with about the same consistence as lanolin, dark yellowish brown in color, and with the characteristic odor of sulphurated organic compounds. The original object aimed at in preparing it was to obtain a body possessing all the useful properties of a remedy of the good old times—oleum lini sulphuratum—without its disadvantages.

The preparation has been used in a number of cases of eczema of all degrees of intensity and extent, in the most different parts of the body. In some of them the usual remedies had been tried in vain. The application of thilanin was followed by alleviation of irritation and itching, and subsequent restoration of the skin to its normal condition and functions. In eczema of the scalp, where cutting the hair very short is not feasible, the ointment must be diluted with oil or aqueous liquids—which it absorbs as well as lanolin—in order to enable it to be brought into intimate contact with the affected parts.

A beneficial influence was also observed upon sycosis, herpes, acne, psoriasis, and other forms of skin disease (Saalfeld). Experience showed that it had a more energetic effect than the usual indifferent remedies (Ung. Hebræ, borovaselin, or borolanolin) while at the same time perfectly non-irritating; on the other hand, it relieves the itching of a number of skin affections.

METHACETINE.

Synonyms : PARA-ACETANISIDINE: PARAOXYMETHYLACETANILIDE.

$C_6H_4.OCH_3.NHCH_3CO.$

A crystalline compound differing from acetanilide in the substitution of a hydrogen atom by the oxymethyl group— OCH_3.

Preparation.—Nitro-phenol is first prepared by the action of melted phenol upon nitric acid (specific gravity 1.34), separation, washing and steam distillation of the oily liquid formed. Orthonitrophenol passes over, and pure paranitrophenol is obtained from the residue by recrystallization from hot concentrated hydrochloric acid. By the action of soda lye, sodium paranitrophenol is formed, and this, by heating with methyl chloride, yields nitranisol. The reduction of nitranisol to anisidine, and the action of glacial acetic acid upon the latter complete the process, the compound being purified by repeated crystallization from boiling water. The principal reactions may be represented as under :—

$$\underset{\text{Phenol}}{C_6H_5HO} + HNO_3 = H_2O + \underset{o\text{- and }p\text{-Nitrophenol.}}{C_6H_4OH\,NO_2}$$

$$\underset{\text{Sodium }p\text{-nitrophenol.}}{C_6H_4ONaNO_2} + CH_3Cl = NaCl + \underset{\text{Nitranisol.}}{C_6H_4OCH_3\,NO_2}$$

$$C_6H_4OCH_3NO_2 + 6H = 2H_2O + \underset{\text{Anisidine.}}{C_6H_4OCH_3\,NH_2}$$

$$C_6H_4OCH_3\,NH_2 + CH_3COOH = H_2O + \underset{p\text{-Acetanisidine.}}{C_6H_4OCH_3NH\,CH_3CO}$$

Physical and Chemical Properties.—Lustrous scaly crystals, free from color (or feebly reddish); odorless and melting at 127° C.; at higher temperatures distills unchanged. Scarcely soluble in water at 15° C. (1:530); readily so in the the same solvent at 100° C. (1:12); the solutions should be neutral. Also abundantly taken up by alcohol, acetone, chloroform, glycerine and fatty oils, especially if warmed; less so by benzene, and only very slightly by carbon bisulphide, petroleum benzin, ether and essential oils.

The absence of sulphates, chlorides and iodides is ensured by the usual tests, and inorganic impurities generally by ignition on platinum foil. The compound should form a

colorless solution with concentrated sulphuric or hydrochloric acid (carbohydrates darken). With concentrated nitric acid it gives an immediate orange color, and on cooling a crystalline yellow nitro-product separates. The distinction of methacetine from acetanilide, phenacetine, and exalgine is detailed under the properties of the last-named body, and in the monograph on acetanilide.

Like acetanilide (*q. v.*) methacetine gives the indophenol reaction. When boiled with an insufficiency of water to form a solution methacetine forms an oily liquid, which on cooling solidifies. Phenacetine similarly treated does not melt.

Medicinal Uses.—This compound was first recommended in 1888 as an antipyretic for children and enteebled persons (Mahnert), having the advantage of exerting no solvent effect upon the red blood corpuscles; it is well-borne, and no malaise, tinnitus, cardiac weakness or exanthem follow its administration (Seidler, Mosler, Heinz and others). The only unpleasant effects are the sometimes violent outbreaks of perspiration, ½ to 1 hour after the dose (Mahnert, Seidler), and a few cases of collapse after comparatively small doses are recorded (Mahnert, Heinz, Seidler). Methacetine has done good service as an antipyretic and analgesic, producing very favorable results also in acute rheumatism. In cases of ileo-typhus, tuberculosis, etc., with moderate fever, reduction to the normal was effected by comparatively small doses, but where the fever was more intense, larger quantities had to be given. The effect appears very soon after the dose (at the most in half an hour), and the fall of temperature lasts for about an hour, rising then again gradually, sometimes with rigors (Mahnert, Seidler, Kapper). According to some observers, the reduced temperature can be maintained by the administration of divided doses of 3 grains (Masius).

METHYLAL.

Synonym: Methylendimethylether.

$CH_2(OCH_3)_2$

One of a group of bodies termed "acetals." This member was first prepared pure in 1839 by Malaguti.

Preparation.—By the interaction of methyl alcohol, manganese dioxide and sulphuric acid, distillation of the product and purification by repeated fractional distillation and removal of water by potash. The reactions consist first in the oxidation of the methyl alcohol to formaldehyde and the reaction of this with undecomposed methyl alcohol, thus :

$$CH_2O + 2CH_3OH = H_2O + CH_2(OCH_3)_2$$

Physical Properties.—A limpid, colorless liquid, with a penetrating ethereal odor, of specific gravity 0.855 and boiling point 42° C. Soluble in water (1:13), in alcohol, ether and in fatty and ethereal oils. Like chloroform it is not easily inflamed. It is not altered by alkalies, but is decomposed by concentrated sulphuric acid. The solutions must be neutral. Aldehyde and methyl alcohol are detected, if present, by the decoloration effected when one drop of volumetric potassium permanganate solution is added to a solution of five drops in three drachms of water, with 10 drops of dilute sulphuric acid.

Medicinal Uses.—Methylal was first recommended as a hypnotic in 1886 (Personali). The first effect was described as a transient period of excitement, on which followed deep and quiet sleep. The respiration was somewhat slowed, the pulse increased in frequency, blood pressure and temperature somewhat reduced, and reflexes weakened. The remedy was principally excreted through the lungs, and hence its effects were only of short duration. Methylal has been employed in mental diseases; in the delirium of alcoholism and in the beginning of simple psychoses with nocturnal excitement it was ineffective (Mairet, Combemale, Lemoine), but proved effective in the later stages of the diseases, in the insomnia of dementia and in progressive paralysis. Subcutaneously, in doses of 1½ minims, diluted with nine parts of water, methylal has been successfully given in delirium tremens; so far as present experience goes it is the best sedative and hypnotic in delirium tremens (v. Krafft-Ebing).

Methylal has been used as an anæsthetic, and externally

in the form of ointments and liniments against pain ; the literature relating to these applications is meagre. It would appear to be effective as an antidote to small quantities of strychnine (Motrokin, Personali), but worse than useless if a fatal dose has been taken (Langgaard).

The average dose as a hypnotic was given as 1¼ drachms, in aqueous solution with syrup or in some viscid vehicle. For some years however little or nothing has been heard of methylal, and it seems to have been entirely displaced by later remedies.

METHYL CHLORIDE.

Synonyms : Chlormethyl ; Monochlormethane.

CH_3Cl.

A gaseous compound first prepared by Berthelot.

Preparation.—By the interaction of molecular proportions methyl alcohol and hydrochloric acid, with or without the addition of chloride of zinc. The gas produced is washed by leading it through water, sulphuric acid, soda solution, then sulphuric acid again, and finally compressing it in metallic cylinders under a pressure of 3 to 7 atmospheres.

Physical and Chemical Properties.—A colorless gas with an ethereal odor; it burns with a greenish flame though it is not highly inflammable. Soluble in one-fourth its volume of water, much more so in ethyl or methyl alcohol, and freely in ether and chloroform. Under a pressure of five atmospheres at normal temperature, or under normal pressure at -25° C., it is a liquid with a specific gravity of 0.9915 (at -23.7° C.), and boiling point of -21° C. This liquid should be neutral to test paper and unaffected by silver nitrate or potassium iodide and starch paste.

Medicinal Uses.—The compressed liquid form of methyl chloride was recommended for use as spray against neuralgia, pruritus, and spinal pains after railway accidents (Debove, Steiner). One writer raised a warning voice to the effect that unless care were taken in its application phlegmones, grangrene, erysipelas and severe pigmentation might occur (Schuchardt), but no other evidence of this kind has been published.

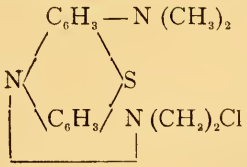
As compressed methyl chloride absorbs a large quantity of heat in reassuming the gaseous condition it has been used to produce local anæsthesia. A stream of the liquid is directed upon a tampon of wool and silk placed over the surface to be anæsthetized; the liquified gas at first saturates the tampon, and then rapidly evaporating therefrom absorbs the heat from the adjacent parts of the body and leaves them bloodless and insensitive. It has been employed thus against local pain, and in minor surgery. When sprayed directly upon the area it is desired to anæsthetise the stream should not be maintained more than two or three seconds at a time, though the application may be repeated at intervals according to the necessities of the case. Under its use in this way minor operations have been very satisfactorily performed, and absolutely without pain (Berezovsky). Over the ether spray it has the advantages of more rapid effects, non-inflammability, and freedom from irritant effects upon the mucous membrane.

DERIVATIVES AND ALLIED COMPOUNDS.

Richardson's compound-liquid is a mixture of ether and chloroform saturated with methyl chloride. It was recommended as a substitute for pure chloroform as an anæsthetic, but does not appear to have any advantages over the latter.

METHYLENE BLUE.

Synonym: TETRAMETHYLTHIONINE CHLORIDE.



A diphenyl amine compound, also classed as an "aniline colol."

Preparation.—By oxidation of dimethylparaphenylenediamine by ferric chloride in the presence of the necessary quantity of sulphuretted hydrogen, or by the interaction of the hydrogen sulphide and nitrosodimethylaniline and oxida-

tion of the product in strong sulpuric acid solution. The patented process consists in oxidation of *p*-amidodimethylaniline in the presence of sodium thiosulphate when *p*-amidodimethylaniline thiosulphonate is formed. From this methylene blue can be obtained in two ways, (α) by mixing with dimethylaniline, treating with chromates and boiling the resultant tetramethylindamine thiosulphonate with zinc chloride solution, or (β) by reduction to *p*-amidodimethylaniline mercaptan and oxidation of this with chromates in the presence of dimethylaniline. Leucomethylene blue (the dihydro additive produce of the base) is actually formed in both these processes, and is easily converted into methylene blue by oxidation.

Physical and Chemical Properties.—The methylene blue (ethylene blue O) of commerce is a hydrochloride or a zinc chloride double salt of the coloring base. The preparation which has been used in medicine was described as free from zinc, being a hydrochloride of the pure base tetramethylthionine. Small indigo colored scaly crystals with a bronze-like tinge, and dark green in transverse fracture. Slightly soluble in water—up to 3 per cent. (Brunner)—forming a deep blue solution, which is changed by sulphuric acid to bright green, and from which strong potash solution throws down a dark violet precipitate. In the presence of alcohol, water takes up more.

Medicinal Uses.—Methylene blue was first applied medicinally in 1890 as an analgesic in neuralgic and rheumatic affections; its use in this way was suggested by its special affinity for the nervous system, particularly for the axial cylinders of the sensible and sensory nerves (Ehrlich and Leppmann). The remedy was given either subcutaneously in doses of ⅓ to 1 grain, or internally in gelatin capsules in doses of 1½ to 8 grains. Good results were obtained in angeiospastic migraine, in simple neuralgia and acute rheumatism (above named authors, Combemale and François), as also in the pleuritic pains of tuberculous patients (Althen). Pains disappeared two hours after doses of 3 grains, and returned only after six to eight hours. No unpleasant effects

of any kind were observed save vomiting in one case (cardiac disease with acute gastric catarrh).

As methylene blue has proved the best stain for the plasmodia found in the blood corpuscles of malarial patients it was also tried against intermittent fever, with pronounced success in 1½-grain doses five times daily. The febrile attacks disappear in the course of the first few days, and the plasmodia from the blood after a week at the most (Guttmann and Ehrlich). The administration must be continued—dose 8 grains *pro die*—eight to ten days after the disappearance of the fever, and in very severe cases even longer. Here also no serious by-effects were observed ; slight vesical irritation or catarrh of the digestive tract sometimes appeared but this was easily combated by the administration of powdered nutmeg, of calcined magnesia, or of linseed tea.

Externally, in aqueous solution for irrigating empyema cavities, in 10 per cent. admixture with cacao-butter (as pencils or suppositories), or internally in substance (capsules or wafers), methylene blue has been given with satisfactory results in various tuberculous conditions. In pulmonary phthisis a dose of 1½ grains was given the first day, increased on the second to 3 grains, on the third to 4½ grains, and so on until 24 grains were taken in the 24 hours. Expectoration diminished and general well-being improved ; the results, compared with those obtained from the creasote treatment, encourage more extended trials (Althen). In pharyngeal tuberculosis the powdered substance was also applied to the affected areas (after cocainisation); in scrofulous swelling of the glands of the neck it was injected in 17 per mille solution. In all cases healing was effected. Most satisfactory results were obtained in endometritis and other diseases of women by combined local (pessaries) and general treatment; a daily dose of 8 grains was never exceeded here.

DERIVATIVES AND ALLIED COMPOUNDS.

Pyoctanin.—Under this name two dye-substances were introduced into medicine during the second half of 1890, on the recommendation of Professor J. Stilling, who carried out

(in association with Dr. J. Wortmann) a series of researches on the antibacterial properties of the aniline dyes. The so-called "blue-pyoctanin" is apparently one or other (or mixtures of two or more) of certain compounds classed as *methyl-violets*, while "yellow-pyoctanin" is one of the group of dyes known as *auramines*. Methyl-violet is tetra-, penta- or hexa-methylpararosaniline, and auramine is an imido-compound oftetramethyldiamidobenzophenone, represented by the formula, $2[(CH_3)_2.N.C_6H_4]C:NH$. Solutions of the blue compound (½ to 4 : 10,000) were recommended in general surgery, and of the yellow for ophthalmic practice. Dusting powders, ointments, and dressings were also introduced into commerce. Early in the history of these compounds there appeared a number of reports, of which some recorded the non-success of the antiseptics, and others warned against irritation and eczema, which might be caused around the points of application (Braunschweig, Mautner, Roeloff, Patrzek). On the other hand favorable results were obtained in nasal diseases (Bresgen, Schemmann, Cholewa), in croup, by inhalation of a 5 per mille solution (Kellerer), in eye diseases, ulcus molle and gummata (Petersen, Wanscher), and in the treatment of tumors (v. Mosetig-Moorhof). Sometimes a cure and in other cases improvement followed the use of pyoctanin in certain malignant tumors (v. Sehlen, Einhorn, Bachmaier, Boas), and its use in this direction calls for further observation and experience.

It seems that the substances introduced as pyoctanin are of variable composition (Liebreich), and probably it would be preferable to use a single definite compound from the same group (methyl violet) specially prepared for medicinal use.

Apyonin (from α privative and $\pi\upsilon o\nu$ pus) was put forward as a rival to pyoctanin in ophthalmic practice. It was described as a yellow crystalline powder, little soluble in water, hot or cold, still less so in ether, but abundantly in alcohol. When carefully heated it sublimed, and at higher temperatures burned away without residue. The concentrated aqueous solution was neutral; its color was altered by neither hydrochloric acid nor nascent oxygen. Potash produced a white precipitate, soluble in alcohol. It has been

affirmed to be identical with yellow pyoctanin, but did not succeed in attracting any attention.

Benzo-phenoneid.—According to the discoverers (Galezowski and Petit) this is a definite compound produced by the decomposition of an aniline dye. It is said to be equal as a germicide to pyoctanin, soluble in 100 parts of water, and neither caustic nor irritant. Good results have been obtained in the treatment of corneal ulcers, purulent keratitis, and other ophthalmic affections.

METHYLENE CHLORIDE.

Synonym : DICHLORMETHANE.

CH_2Cl_2

Preparation —By the action of chlorine on marsh gas, on monochlormethane or on diiodmethane. Also more practically by the reduction of chloroform (in alcoholic solution) by zinc and hydrochloric acid, the product being mixed with water, the specifically heavier liquid separated and purified by successive treatment with soda solution, sulphuric acid, water, chloride of calcium and fractional distillation.

Physical and Chemical Properties.—A colorless liquid resembling chloroform in odor and solubility; specific gravity, 1.36 at 15° C.; boiling point, 41.6° C. Not readily inflammable, though the vapors burn with a green-edged flame. When pure, methylene chloride is decomposed by light, similarly to chloroform, and the addition of a small proportion of absolute alcohol is therefore recommended.

Chloroform, if present, raises the specific gravity. Ethyl or methyl alcohol added as well as chloroform to prevent detection by the gravity are separated by shaking with water, and the dried and redistilled methylene chloride examined again. The separated washing water should give no turbidity with silver nitrate (chlorinated decomposition products) nor blue color with zinc iodide and starch (chlorine); it should also be neutral to test paper (hydrochloric acid).

Medicinal Uses.—This compound was recommended as a substitute for chloroform, being expected to be less dangerous than the latter owing to its less chlorinated constitu-

tion (Eichholz and Geuther). It was particularly used and recommended in gynæcology, but other physiologists (Nussbaum, Breisky and Kapeller) record the production of clonic spasms, nervous disturbances, and even death after its use.

Methylene chloride has also been used in the form of spray as a local anæsthetic.

DERIVATIVES AND ALLIED COMPOUNDS.

English methylene chloride, or *méthylène*, is a mixture of ethyl ether and methylene chloride; it must be carefully distinguished from the definite chemical compound described above. Was recommended as a safe anæsthetic in quantities of about 1 to 2 drachms for minor, or 2 to 6 drachms for larger operations (Richardson), but is not so free from danger as its originator believed; deaths after its use have been recorded (Lawson-Tait).

A mixture of chloroform and methyl chloride has also figured in commerce as "methylene chloride."

NAPHTALENE.

Synonym: NAPHTHALIN.

$C_{10}H_8$.

The typical and simplest known member of the so-called naphtalene series of hydrocarbons, with the general formula C_nH_{2n-12}.

Preparation.—Abundantly present in the fraction which comes over between 180°—220°C in the distillation of coal tar; it separates from this fraction on cooling as a brown mass and is purified by the action of soda and sulphuric acid followed by repeated sublimation. Synthetically obtained by the action of heat on phenylbutylene—a product of the action of sodium on a mixture of benzyl chloride and allyl iodide.

Physical and Chemical Properties.—Large lustrous scales, with a penetrating odor, and a burning aromatic taste; it melts at 80°C., readily sublimes and boils at 218°C. It readily passes over with the vapor of water. Naphtalene is insoluble in water, difficultly soluble in cold, readily in hot alcohol, in ether, chloroform, fatty and essential oils, and in

hydrochloric and acetic acid without forming salts. By oxidation it is readily converted into phtalic acid, $C_6H_4(COOH)_2$, from which benzoic acid and certain important coloring agents such as phenolphtalein and eosin are prepared.

Naphtalene should be colorless and without action on moist blue litmus paper; on platinum foil it should burn away without residue. If quite pure it remains colorless, and the physical constants are as given above. Further, it must dissolve in concentrated sulphuric acid when warmed gently without color.

Medicinal Uses.—Naphtalene has been employed in medicine chiefly in virtue of its antiseptic and disinfectant properties. Externally in 10 to 12 per cent. solution in linseed or olive oil against itch (Fürbringer), and in ointment form (5 to 10 per cent.) in the treatment of a series of skin diseases, as eczema chron., psoriasis, lepra vulgaris, etc. Has also found application as dusting powder (with 2½ per cent. of bergamot oil to cover the odor), as spray (ethereal solution), gauze and wool in the treatment of wounds.

Internally very varied results have been yielded, possibly due in some measure to impurity in some of the specimens; some observers record a dangerous action on the kidneys (Magnus), others that in large doses it destroys the red blood corpuscles (Panas, Dorr, Hess, Kolinski). Excellent results have sometimes followed its use in 5-grain doses against typhus, fever and diarrhœa being reduced and the duration of the disease lessened (Wolff). Naphtalene has also been recommended as a safe and reliable anthelmintic in doses of 15 grains (children 5 to 8 grains), with castor oil and bergamot as a corrective (Mirovitch). Inhalations have done good service in the treatment of whooping cough; only consumptives are not benefited—(of diagnostic value)—(Chavernec). Recommended further as an expectorant in diseases of the respiratory tract, in pills, powders and lozenges, and for irrigation (Rossbach).

Naphtalene can be made into pills by mixing with half its weight of powdered marshmallow root and massing with mucilage. A coating of flexible collodion is preferable to keratin (Bernbeck).

Being poisonous to lower forms of life naphtalene is employed as a preservative of collections, clothes, etc., against the attacks of insects and the like. A small quantity of camphor is said to largely cover the odor of the compound —sometimes considered disagreeable—without reducing its value as a preventive of moth, etc.

NAPHTOL.

Synonym : Iso- or β-Naphtol.

$C_{10}H_7OH$

A crystalline compound resulting from the substitution of a hydrogen atom in the double ringed naphtalene $C_{10}H_8$ by a hydroxyl group.

Preparation.—By the action of fuming sulphuric acid on naphtalene for several hours at 200° C. The β-naphtalene sulphonate which is chiefly produced is dissolved in water, neutralized with chalk, the calcium salt crystallized out (the α-salt is more soluble), dissolved in water, converted into sodium salt and the latter decomposed by melted soda as shown under :

$$C_{10}H_7SO_3Na + NaOH = Na_2SO_3 + C_{10}H_7OH$$

Sodium naphtalenesulphonate — Naphtol.

The product is purified by pressure, distillation and recrystallization from hot water, or from petroleum ether (from which it separates in scales).

Physical and Chemical Properties.—Colorless, lustrous, scaly crystals (or a white crystalline powder), with a faint phenoloid odor, and a transient burning taste ; it melts at 123° C., and boils at 286° C. Soluble in alcohol, ether, benzene, chloroform, oils and alkaline liquids. Scarcely soluble in cold, fairly so in hot water (nearly six grains in ℥j.), forming a liquid which, on the addition of ammonia or soda, exhibits a bluish-violet fluorescence, and on the addition of chlorine water a white turbidity changed by ammonia to a clear green, and later, to brown solution. With ferric chloride the hot aqueous solution gives a green tint (violet if α-naphtol be present), but it is unaffected by ferrous sulphate or lead acetate. In the presence of boric acid a solution of the strength of 1 grain in 2 ounces of lukewarm water may be

made (Anotta), which acts more energetically as an antiseptic than either boric acid or naphtol alone.

Inorganic impurities are detected by combustion on platinum foil, and α-naphtol by ferric chloride (*v. supra*). Impure specimens are said to be distinguished by darkening when exposed to light. (*cf.* **Betol.**)

α and β-naphtol are also distinguished by the color formed on melting with 25 times their weight of chloral hydrate; α-naphtol gives an intense ruby-red, not fluorescent, and β-naphtol a pure blue;—40 grains of chloral hydrate, and 5 drops of hydrochloric acid dissolve 1½ grains of α-naphtol with an intense non-transparent dark greenish-blue color, or the same quantity of β-naphtol to an intense transparent yellow (Lustgarten, Reuter). Richardson uses a test solution made by dissolving one grain of *p*-aniline sulphonic acid in water, to which one drachm of normal soda solution had been added. Then one drachm of normal sulphuric acid and ⅓grain of sodium nitrite are also added. The naphtols are dissolved in water containing a few drops of normal soda-lye; α-naphtol gives a dark blood-red, and β-naphtol a reddish yellow. By salting out the colors the difference between them is rendered more pronounced. Dilute sulphuric acid does not affect the β-color, but changes the α-color to dark brown.

Medicinal Uses.—β-naphtol was first introduced into medicine as an antiseptic externally in 1881 (Kaposi). Symptoms of poisoning have been observed after its use (Lesser, Neisser), but these were attributed to impurities in the specimen employed (Shoemaker). An exhaustive pharmacological examination of β-naphtol was carried out in 1888 (Willenz), which showed that the compound is not without poisonous effects on animals, though these are less pronounced than some authors believed. It has been employed against skin diseases, organic and parasitic, in ointment form (3 to 10 per cent.) and in alcoholic solution (2 to 10 per cent.). Also in chronic suppurative affections of the middle ear in substance or alcoholic solution (Hand). Internally, doses of 5 to 8 grains, several times a day, have been recommended for intestinal disinfection, especially in typhus (Robin and

others). In chronic diarrhœa very good results have followed its administration (Ewald).

In 1 per mille solution β-naphtol has been highly spoken of as a preservative for anatomical preparations; its powerful bactericidal properties have been established by repeated experiment (Willenz, Bouchard).

DERIVATIVES AND ALLIED COMPOUNDS.

Camphorated β-naphtol is a syrupy liquid used with great success in the antiseptic treatment of boils, coryza, angina diphtheritica, and tuberculosis (Fernet). Against the latter it was given by intraparenchymatous injection in doses of 2 grains mixed with oil. Cures were effected in 21 out of 27 cases of tuberculous glands by emptying any abscess formed, and injecting 7 to 8 drops of camphorated naphtol, repeated every two days (Reboul, Nelaton). The pain caused by painting the diseased parts with camphor-naphtol may be alleviated by the addition of cocaine.

Hydronaphtol is an American product, described as a derivative of β-naphtol, obtained by reduction, and put forward as an antiseptic and disinfectant free from the toxic action of the parent compound. As to the actual nature of the substance quite variant opinions have been expressed, and it seems to be still open to doubt. Dr. M. Dockrell has used it against tinea tonsurans in the form of plaster, a chief indication being to prevent the access of air (oxygen). The affected area was shaved, washed with hydronaphtol soap, and hot water, covered with over-lapping strips of 10 per cent. hydronaphtol plaster, and the outside margin of the latter painted over with melted hydronaphtol jelly. At the end of four days the plaster is removed and put on fresh. Two repetitions were sufficient to cure (Dockrell). Successfully employed in the treatment of enteric fever and diarrhœa in doses of two or three grains in capsule, or suspended in milk every two hours. In typhoid, 3 or even 4 grains were given to begin with every two hours. As it sometimes interfered with digestion, it has been suggested that it might be given in pills coated with keratin (Clarke). Recommended for external use in solution, one part of hydronaphtol dis-

solved in 10 parts of rectified spirit, to which sufficient glycerine is added to make 1 per cent. solution. In this form the antiseptic properties of the body were well marked (Bryce).

Microcidin—This substance, recommended as an antiseptic (Polaillon), is practically sodium naphtol, being prepared by melting β-naphtol with half its weight of sodium hydrate and allowing to cool. A whitish powder is obtained which is soluble in 3 parts of water. For the purposes of wound treatment solutions of 0.3 to 0.5 per cent. of microcidin are recommended; these solutions are non-caustic, non-poisonous, and in activity are ten times as strong as boric acid in the same dilution (Berlioz). Microcidin is also recommended for internal use; it reduces febrile temperature and has an antiseptic effect: the greater part is excreted by the kidneys.

Benzonaphtol, or *β-naphtol benzoate*, analogous to betol (β-naphtol salicylate), is prepared by the action of benzoyl chloride on β-naphtol (equal quantities or an excess of the former) in a sand bath. Reaction begins at 125° C. and at 170° C. is complete in half an hour; it may be expressed as follows:

$$\underset{\text{Benzoyl chloride.}}{C_6H_5COCl} + C_{10}H_7OH = HCl + \underset{\text{Benzonaphtol.}}{C_6H_5CO_2C_{10}H_7}.$$

On cooling the mass crystallizes to a hard cake, from which the benzonaphtol is extracted by boiling alcohol, or the mass broken up into small fragments is digested with twice its weight of a 2 per cent. soda solution and the operation repeated until no further reaction for free naphtol is given (blue color by chloroform and potash).

Benzonaphtol crystallizes in long needles, or forms a white crystalline powder, free from taste and odor, insoluble in water at ordinary temperatures; it melts at 110°. A hot spirituous solution with an equal volume of nitric acid should give no cherry-red color on addition of a few drops of acid mercuric nitrate (free naphtol).

In the intestinal tract the compound is split up into its constituents and the naphtol remains in the urine while the benzoic acid partly converted into hippuric acid is excreted with the urine. Given internally to animals it causes diu-

resis, lowering of temperature, and of cardiac and respiratory action (Dominici). Excellent results were obtained from the experiments on human beings, and the excreted urine was considerably less poisonous than that of β-naphtol (Gilbert). The compound was given in doses of 1¼ drms. (children, 30 grains) *pro die* in frequently repeated small portions either in powders or emulsion.

Di-iod-β-naphtol, or *Naphtol-aristol.*—An aqueous solution of 2.4 parts each of iodine and iodide of potassium is mixed with a solution of 11 parts of β-naphtol and 4 parts of sodium carbonate; to the mixed liquid a solution of sodium hypochlorite is added, when a greenish yellow substance is thrown down which is washed and dried in the dark. It is odorless and tasteless, insoluble in water, sparingly taken up by ether, by alcohol or acetic acid, freely so by chloroform; when heated it evolves violet fumes. The preparation is put forward as an antiseptic (Braille).

Naphtopyrin is one of the several phenol compounds of antipyrine experimentally prepared during the past year or so. It does not appear to have been yet employed in medicine. Naphtopyrin was made from β-naphtol by prolonged trituration with twice its weight of antipyrine. It forms a tough body, insoluble in water, soluble in alcohol and ether; on keeping for a length of time it slowly assumes a crystalline form.

α-Naphtol, isomeric with the β-compound, was recommended in 1888 as an antiseptic of great power and relative harmlessness (Maximowitsch). In solution of 0.1 to 0.25 per mille it acted as a kolyseptic to the spores of the typhoid and tubercle bacillus. In this respect it was one and a half times as strong as β-naphtol but three times less aggressive to the skin, etc.; 1½ grains prevented alcoholic fermentation in a litre of grape sugar solution.

α-Naphtol has been recommended as a test for sugar in urine, the reaction being utilized as follows:—one drop of the urine with 1 drop of a 10 per cent. solution of α-naphtol in chloroform is placed in a test tube with 1 ccm. (about 15 min.) of water; concentrated sulphuric acid is then carefully poured in so that the chloroformic solution floats on it. A

beautiful violet ring is formed at the surface of contact of the two fluids if only 0.03 per cent. of sugar be present (Molisch and Luther). It is important that *all* the reagents be pure and that the urine be diluted with ten times the volume of water. The reaction is also available for use quantitatively.

α-Oxynaphtoic acid ($C_{10}H_6OH\ COOH$) is obtained by a process analogous to that employed in the preparation of synthetical salicylic acid, viz.: by the action of carbonic acid gas upon sodium α-naphtol. It occurs in colorless acicular crystals with an odor like that of naphtol; m. p. 185° C. This acid is difficultly soluble in cold, more readily in hot water; alcohol and ether take up 10 per cent. and glycerine 0.5 per cent. Forms soluble salts with the alkalies or alkaline carbonates. Recommended as an antiseptic and disinfectant (Ellenberger and Hofmeister, Luebbert), and used in skin diseases and scabies as a ½ per cent. collodion, or with lanolin. Also applied as wool and 10 per cent. ointment (Helbig).

OREXINE HYDROCHLORIDE.

Synonym: PHENYLDIHYDROCHINAZOLINE HYDROCHLORIDE.

$$C_6H_4 \begin{cases} N\ CH \\ CH_2N\ C_6H_5HCl \end{cases}$$

A complex derivative of chinoline, first introduced into medicine in 1890.

Physical and Chemical Properties.—Colorless, or very slightly colored, odorless, lustrous, lanceolate crystals, containing two molecules of water, which effloresce on exposure. Its taste is bitter and pungent, approaching to the caustic, and freely soluble in hot water. It powerfully irritates the mucous membrane of the nose.

Medicinal Uses.—Orexine was put forward, in the first instance, as a stomachic of marked activity exerting simultaneously a stimulant action on the appetite and a tonic influence on the digestive organs (Penzoldt). Being a synthetical remedy that was neither an antipyretic nor an antiseptic, but belonged to an entirely different class of medicaments, orexine attracted a good deal of attention and its literature was rapidly added to. It may be said that the majority of ob-

servers more or less strongly corroborated the statements of the original author (Glueckziegel, Hoffmann, Kronfeld, Reichmann, Umpfenbach, Kothar, Boas, Matthes), though there have not been wanting others who set less value upon the remedy or altogether denied its usefulness (Imredy, Martius, Podgorski, Battistini, Svirelin). The lack of satisfactory results recorded in some instances has been ascribed to the non-disintegration of the gelatine-coated pills in which it was prescribed. Experiment and clinical observation have shown that such pills may remain in the stomach for hours without being in the least affected. Hence it is recommended to give the remedy in wafer. In doses of 4 to 8 grains it shortens the process of gastric digestion in both healthy persons and patients, producing the more rapid appearance and increase of the hydrochloric acid secretion. It appears to be particularly useful in the anorexia which follows on the shock of major operations, in that of tuberculosis (when not too far advanced), of anæmia and in chronic gastric catarrh. In diseases of the stomach, such as acute catarrh, ulcer and the like, where the viscus should be protected from irritating agents, it is not suitable.

As already indicated orexine should not be prescribed in pill form, but preferably in wafer and accompanied by a copious draft of some liquid (beef-tea, cocoa) in order to prevent any local irritant action.

PARALDEHYDE.

Synonyms : PARALDEHYDUM ; ELALDEHYDE.

$$CH_3CH \begin{Bmatrix} OCHCH_3 \\ OCHCH_3 \end{Bmatrix} O$$

A product of the condensation of three molecules of ordinary ethyl aldehyde.

Preparation.—Ordinary aldehyde is treated at a medium temperature with small quantities of hydrochloric acid, carbon oxychloride, sulphurous anhyride (sulphuric acid causes explosive ebullition), or zinc chloride. The temperature of the liquid rises, and almost complete conversion into paraldehyde occurs. Purification is effected by repeatedly freezing out and rectifying.

Physical and Chemical Properties.—According to the B. P. Additions (1890) paraldehyde is a clear colorless liquid, having a characteristic ethereal odor, and a burning, and afterwards cooling taste. Specific gravity 0.998. Boiling point 255.2° F. (124° C.) At 50° F. (10° C.) it begins to congeal to a clear crystalline mass. Miscible in all proportions with rectified spirit or ether. One part dissolves in 10 of water at 60° F. (15.5° C.), forming a neutral solution ; it is less soluble in hot water. The requirement that no coloration should be produced when it stands for two hours mixed with a solution of potash or soda is presumably designed to detect aldehyde if present ; freedom from sulphates, chlorides, etc., originating from the method of preparation, is ensured by the statement that neither chloride of barium nor nitrate of silver must produce a precipitate.

It may be pointed out that even pure paraldehyde may be cooled considerably below 10° C. without solidifying unless it be stirred while the temperature is falling. Specimens containing alcohol or aldehyde may remain liquid at -5° C. From a cold saturated aqueous solution containing 11¾ per cent. of paraldehyde about half of the dissolved compound separates at 100° C. Amyl or valer-aldehyde are detected by the odor of the residue left from evaporation of 2 or 3 drachms on the water bath.

As paraldehyde is readily converted into acetic acid by oxidation, and even by the action of atmospheric oxygen, it will not often or long be absolutely neutral. It has been, therefore, provided by the P. G. Ed. III. that 1ccm. with an equal volume of acid-free alcohol should not react acid after the addition of 1 drop of normal potash solution.

Medicinal Uses.—Paraldehyde was introduced into medicine about 1883 as a hypnotic and sedative. Physiologically its action is characterized by the absence of action on the heart. It has a strong reducing effect upon the blood, like all aldehydes, and this influence precedes the narcotic action (Froehner). Paraldehyde was specially recommended as a substitute for chloral where this agent was contraindicated or did not produce satisfactory results (Cervello, Krafft-Ebing). Experiments made quite recently have shown that

the presence of paraldehyde, even in minute proportions, accelerates the digestion of fibrin, and that the greater the amount present the more rapid is the digestion (Gordon).

Single doses of 40 to 60 min. produce sleep in five to fifteen minutes; half a drachm every three hours produced within half an hour two hours' sleep; 20 min. every four hours for fourteen days produced better sleep at night—not during the day (Therapeutic Committee, Brit. Med. Assoc.) Paraldehyde may be prescribed with tincture of orange or some other bitter tincture; it can also be taken in some form of spirit. An emulsion is prepared by making a thick mucilage with 2 drms of powdered gum arabic and adding some of the paraldehyde; having stirred until the mixture is homogeneous, a little water and more paraldehyde are added. One may proceed in this way until as much of the hypnotic has been added as was taken of gum (in this case, therefore, two drachms) making up the mixture to a definite volume (*e. g.*, four ounces) with flavoring agents and water.

The remedy has also been administered in suppositories and subcutaneously, but there is seldom need to resort to these forms as it is promptly absorbed from the stomach.

DERIVATIVES AND ALLIED COMPOUNDS.

Metaldehyde [$(C_2H_4O)n$] is formed by the action of polymerising agents upon aldehyde at a temperature below 0°C. It is a white crystalline body, insoluble in water, but freely taken up by hot alcohol and ether. When heated it sublimes without melting between 112° to 115° C., being at the same time partially decomposed. Metaldehyde has been credited with hypnotic properties.

Sulphaldehyde was described in the early part of 1891 as obtained by the action of sulphuretted hydrogen upon ordinary aldehyde. It forms, according to the note published, an oily liquid with a repulsive odor, solidifying at -8°, and melting again at -2°C. Treated with acids it seems to undergo polymerisation, like aldehyde, forming the solid sulpho, or thio-paraldehyde. According to Luisini sulphaldehyde produced a deep and quiet sleep in frogs and rabbits, and proved more powerful than paraldehyde: ⅓ min.

producing the same effect as nearly ½ min. of the latter. Luisini's recommendation does not seem to have at all attracted attention, at last nothing further has appeared.

PENTAL.

Synonym : TRIMETHYLETHYLENE ; *β*-ISOAMYLENE.

$(CH_3)_2$ C. CH. CH_3

An impure amylene was described in 1844 (Balard) and used in 1856-57, after which it fell into oblivion.

Preparation.—Amyl alcohol produced by fermentation, is distilled with zinc chloride; ordinary amylene is obtained which consists of trimethylethylene (about 50 per cent.) with pentane, C_5H_{12} (boiling at 29° C.), together with varying quantities of *α* and *γ*-amylene. If shaken in the cold (-20° C.) with sulphuric acid which is diluted with ½ to 1 volume of water the trimethylethylene dissolves (as also does any *γ*-amylene present) to amyl-sulphuric acid, which after dilution with water yields on distillation pure trimethylethylene and tertiary amyl alcohol. From the latter the pental is separated by fractional distillation. Also obtained from amylene hydrate by the action of acids.

Physical and Chemical Properties.—A colorless liquid of low specific gravity (0.62), insoluble in water, but miscible in all proportions with alcohol, chloroform or ether. Pental boils at 38° C., and is highly inflammable; being characterized by considerable stability it does not decompose on exposure to light and air.

Medicinal Uses.—Pental was introduced towards the close of 1891 as an anæsthetic especially suitable for use in dental surgery. The narcosis sets in after 1 to 1½ minutes, although, of course, this time varies, according to the character of the patients, being shorter when they are quiet and breathe regularly. The anæsthesia appears to be complete before consciousness is altogether lost, and the awakening is quite gradual. Neither during the narcosis nor afterwards are any unpleasant symptoms observed (Hollaender, von Mering, Weber, Mebes, von Rogner). Over ethyl bromide, the chief liquid anæsthetic in use, it seems to have the advantage of greater stability and freedom from irritant effects; it

never produces the cramp-like spasms of the bromide (Hollaender).

Pental is best administered by the apparatus known as Funker's (which is provided with an India-rubber ball for forcing air through the liquid), but for quite short operations a well-fitting chloroform mask (Skinner or Esmarch) may be made available for the purpose by covering it with a few folds of flannel and finally with some impermeable material, —2 to 3 drachms of pental are generally sufficient to produce sufficient narcosis for ordinary operations.

PHENACETINE.

Synonyms : PHENACETINUM ; ACETPHENETIDINE.

$C_6H_4OC_2H_5NHCH_3CO.$

A crystalline compound closely allied in chemical constitution to acetanilide and methacetine.

Preparation.—Sodium para-nitrophenol (*v.* Preparation of **Methacetine**) is converted by the action of ethyl iodide into *p.*-nitrophenetol, the latter reduced to *p.*-amidophenetol (*p.*-phenetidine), which by prolonged boiling with glacial acetic acid yields phenacetine. The equations are (*v.* also **Methacetine**) :—

$$C_6H_4ONa\,NO_2 + C_2H_5I = NaI + C_6H_4OC_2H_5NO_2$$

Sodium *p* -nitrophenol — *p* -Nitrophenetol

$$C_6H_4OC_2H_5NO_2 + 6H = 2H_2O + C_6H_4OC_2H_5NH_2$$

p.-Phenetidine.

$$C_6H_4OC_2H_5NH_2 + CH_3COOH = H_2O + C_6H_4OC_2H_5NHCH_3CO.$$

Phenacetine.

Physical and Chemical Properties.—The B. P. Addendum describes phenacetine as occuring in colorless, tasteless, inodorous, glistening, scaly crystals, melting at 275° F. (135° C.), sparingly soluble in cold, more freely in boiling-water (1:70, P. G.) and in about 16 fluid parts of rect. spirit.

Phenacetine is officially identified by the production of a deep red color when chromic acid is added to a cooled and filtered solution of 1 grain in 20 minims af hydrochloric acid diluted with ten times its volume of water (Ritsert). Its freedom from acetanilide is ensured by the iso-nitrile test, and by providing that a cold saturated aqueous solution

shall not become turbid on addition of bromine water. Lastly, sulphuric acid must dissolve it without color, and heated with free access of air "it burns leaving no residue."

The method of distinguishing phenacetine from similarly constituted bodies is described under exalgine, acetanilide, and methacetine (*q. v.*). Like the two latter, acet-*p.*-phenetidine gives the indophenol reaction. For the detection of 2 or more per cent. of acetanilide in phenacetine, Schroeder recommended boiling 8 grains with about 15 minims of water, cooling, filtering, boiling the filtrate with nitrous acid (or a mixture of potassium nitrite and dilute nitric acid), adding a few drops of Plugge's reagent (a solution of mercurous nitrate containing nitrous acid), and boiling again. In the presence of two or more per cent. of acetanilide the liquid assumes a red color, due to the production of an azo dye.

A later test consists in covering finely-powdered phenacetine with 10 to 12 per cent. nitric acid and heating to boiling; an intense yellow nitro compound is formed and on cooling partly separates in yellow needles. Antipyrine and acetanilide are unaffected under the same conditions (Autenrieth and Hinsberg).

When 40 grains of chloral hydrate are melted in a water bath, 8 grains of phenacetine added, and the whole shaken together, solution occurs which in the presence of only traces of paraphenetidine is colored immediately violet, reddish or bluish in tint, according to the proportion of the impurity present (Reuter).

Further, phenacetine, free from phenetidine, which, under the same conditions, remains colorless, even when warmed, for at least five minutes, gives a pink-colored solution after prolonged digestion (identity). A less delicate test is a dilute aqueous iodine solution (1 : 20,000); 8 grains of phenacetine are shaken with 1½ drachms of this solution, and the liquid filtered; a pure compound yields a colorless filtrate (a pink tint=paraphenetidine). Goldmann uses a solution of 8 grains of phenacetine in ½ drachm of spirit; to this the 1½ drachms of iodine solution is added, and the liquid, with the separated phenacetine, boiled till solution is effected, which is pink if traces of *p.*-phenetidine be present.

Medicinal Uses.—Phenacetine was first recommended as an antifebrile for use in medicine in 1887 (Hinsberg and Kast), since when its literature has attained large dimensions. It has been given in phthisis, typhus, polyarthritis (Collischonn, Rifat), peritonitis, endocarditis, abdominal typhus (Kartschewski), etc., with success, and has also made a reputation as an antineuralgic in vasomotor neuroses in the lancinating pains of tabes of neuralgia and hemicrania (Kobler, Hoppe, Guttmann, Lépine, Dujardin-Beaumetz, Mueller, Mahnert and others). Success followed its use in the whooping cough of children (Michaelis, Kratz, Heimann, Irwin), and in epidemic influenza both as a prophylactic and remedy (Wolff, Rathgen, Hallam, Cleveland, Weed, Henry).

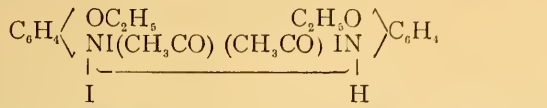
The action of phenacetine seems to be free from collapse and unpleasant by-effects generally; like most of the synthetical antipyretics its antifebrile effects are accompanied by more or less profuse perspiration. When fever is accompanied by unrest, sleeplessness, etc., phenacetine has been found to reduce the high temperature and produce quiet sleep without being followed by headache.

The dose as an antipyretic is 8 to 12 grains hourly or every two hours as may be necessary. As an antineuralgic and against rheumatism 15 grains are given, repeated if required until 1½ drachms have been taken in the twenty-four hours. It has been given with benefit in 2 grain doses combined with 12 grains of citrate of caffeine against migraine. Best prescribed and dispensed in powders or readily disintegrating tablets.

DERIVATIVES AND ALLIED COMPOUNDS.

Iodophenine.—If to a cold saturated aqueous solution of phenacetine, a solution of iodine in potassium iodide, or bromide water be added, or if chlorine be led in to saturation, brown, yellow or greenish solutions are obtained which also remain clear on long standing. It is, however, otherwise if to these solutions hydrochloric acid be added, or if the acid be added before the halogen; under these conditions iodine yields an abundant precipitate. For preparation on the large scale the phenacetine is dissolved in glacial acetic acid and to that solution the hydrochloric acid, water, and solution of

iodine in potassium iodide and water are added. The product, believed to be represented by the formula :—

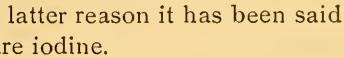


occurs in fine crystals similar in form to those of potassium permanganate; it has a feeble iodine-like odor, a coarse burning taste, and colors the skin yellow. M. p. 130° to 131° with decomposition. Soluble in glacial acetic acid, boiling hydrochloric acid, and in alcohol. Heated or even simply mixed with water iodine is set free (Siebel).

Owing to the looseness with which iodine is held in the compound it exerts marked antiseptic properties (Wittkowsky) and, indeed, has the irritating effects of free iodine (Siebel). For the latter reason it has been said to have no advantages over pure iodine.

Salicyl-, Benzoyl-, and Anisyl-Phenetidine. These derivatives of phenetidine are obtained by the action of the respective acids upon the base in the presence of phosphorous chloride or phosphoric oxychloride; their formulæ correspond exactly to that of phenacetine with the groups $CO.C_6H_4.OH$, COC_6H_5 and $CO.C_6H_4.OCH_3$ respectively, replacing CH_3CO. All three are physiologically inert, in consonance with the indications of recent research showing that the introduction of acid groups into the molecule of the synthetical antifebriles deprives them of their antipyretic virtues (Ehrlich, Aronson). Although, therefore, the first named under the abbreviated title "saliphen"—not to be confounded with salophen (*q. v.*)—was introduced in 1890, none of the compounds have more than a scientific interest.

Thymacetin. This is another substance closely allied to phenacetine, represented by the formula :—



It occurs as a white crystalline powder, which dissolves with difficulty in water. It is said to act as a hypnotic in doses of 5 to 15 grains, and to be, so far as present experiments go, without toxic action on warm-blooded animals.

PHENOCOLL HYDROCHLORIDE.

$$C_6H_4 \begin{cases} OC_2H_5 \\ NHCO.CH_2NH_2HCl. \end{cases}$$

One of the latest additions to the numerous class of antipyretics, distinguished by its comparatively free solubility; is chemically closely related to phenacetine.

Preparation.—By the interaction of phenetidine (paraamidophenetol) and glycocoll or amidoacetic acid. The reaction may be expressed by the following equation:—

$$\underset{\text{Phenetidin.}}{C_6H_4\begin{cases} OC_2H_5 \\ NH_2 \end{cases}} + \underset{\text{Glycocoll.}}{HOOCCH_2NH_2} = \underset{\text{Phenocoll.}}{C_6H_4\begin{cases} OC_2H_5 \\ NH.COCH_2NH_2 \end{cases}} + H_2O$$

The possibility of forming salts is due to the presence of the amide group.

Physical and Chemical Properties.—Phenocoll hydrochloride occurs in the form of a white micro-crystalline powder, soluble, at 17°C., in about 16 parts of water, and forming a neutral solution. From hot water it crystallizes in cubes similarly to antipyrine, from alcohol, in which it is only freely soluble when heated, in needles. Ammonia, the fixed alkalies, and their carbonates throw down the pure base, from a solution of the hydrochloride, in the form of white-matted needles, with one molecule of water of crystallization.

The anhydrous base melts at 100.5° C., but the compound with water at 95° C. Phenocoll is very difficultly soluble in cold, but readily in hot water; it is freely taken up by alcohol, but very little by ether, benzene and chloroform. Dilute solution of the alkalies and their carbonates, and dilute acids, even though boiling, do not readily decompose the base; after prolonged treatment in this way it partially splits up into phenetidine and glycocoll.

Medicinal Uses.—The difficulty referred to in a previous monograph (*v.* Salicylphenetidine) of preparing soluble antipyretics by the introduction of acid groups was overcome in the case of phenocoll by the substitution of a

basic group, viz., that of glycocoll. Physiologically the compound appears to have a marked advantage over nearly all synthetical antipyretics of the aromatic series, in that it has no injurious effect upon the blood corpuscles even when directly brought into contract with them (Kobert, von Mering). It has an effect upon the respiratory centres (Ott). As would be expected from this fact the action of the compound has proved safe, save in the case of emaciated consumptives, without unpleasant by-effects; albumen has not been observed in the urine of patients. Satisfactory results are recorded from its employment as an antifebrile in phthisis and other pulmonary affections, in ileotyphus, etc. (Herzog, von Mering, Hertel, Jacobi, Cohnheim), as an antirheumatic especially in acute forms (Hertel, Cohnheim), and as an antineuralgic (Herzog, Aronson, Cohnheim.)

Given in 8 grain doses when the febrile temperature fluctuates between 39° and 40.5° a reduction of about 2° is obtained accompanied by more or less profuse perspiration; in isolated cases a dose of 8 grains has been followed by a fall of 4° (Cohnheim). In neuralgia small single doses are not so effective as 8 grains three times a day; phenocoll is not indicated in cases of hysterical origin. In acute rheumatism the same single dose was order three to seven times a day; a very rapid effect was produced upon the pain and swelling.

Phenocoll hydrochloride may be prescribed as powder, in capsules, or merely in aqueous solution (℈ j : ℥ iv.) with or without correctives. Patients do not complain of the slightly bitter taste of the remedy.

DERIVATIVES AND ALLIED COMPOUNDS.

Other salts of phenocoll have also been described, but so far have not been therapeutically employed. The *carbonate* is an almost tasteless, bulky powder, readily dissolved by weak acids, and the *salicylate* crystallizes from hot water, in which it is very soluble, in long needles. It has a sweetish not-unpleasant taste, and would probably combine the therapeutical properties of phenocoll and salicylic acid. An *acetate*, soluble in 3½ parts of water, is also known.

PIPERAZINE.

Synonyms: Piperazidine; Ethylenimine; Diethylendiamine; Dispermine.

$C_4H_{10}N_2$

A synthetical compound primarily intended to replace spermine, but found to be a different body in both chemical and physiological characters.

Preparation.—Piperazine is formed from the action of ammonia on ethylene bromide or chloride. In this way the salts of a mixture of bases is obtained consisting of ethylene diamine, a proportion of high-boiling bases such as triethylene diamine, diethylene triamine, tetrethylene triamine, and of a small quantity of diethylene diamine. The mixture of bases fractionated, yields a fraction between 130° and 180° C., from which on cooling the diethylene diamine separates (Hofmann).

By a patented process it is isolated by the conversion of the diethylene diamine into dinitrosopiperazine, by the action of a nitrite. This compound is difficultly soluble in cold water, crystallizes in scales, and gives, when treated with hydrochloric acid or reducing agents, hydrochloride of piperazine with nitrous acid or ammonia.

Physical and Chemical Properties.—Piperazine is solid; it melts at 104° to 107° C., and boils at 145°. It is extraordinarily readily soluble in water, and can therefore be applied subcutaneously. Crystallized from water it forms glassy, lustrous tables. From the air it greedily absorbs water and carbon dioxide, and liquefies in so doing. The aqueous solution is almost tasteless, and has a strongly alkaline, but non-caustic reaction. The hydrochlorate of piperazine is also very easily soluble in water, more difficultly in alcohol; it crystallizes in silky, lustrous, lanceolate forms.

The base is unaffected by aqueous chromic acid, or fuming sulphuric acid, even if heated to 110°; permanganate gradually oxidizes the base in the cold.

Piperazine may be detected in the urine, by adding a few drops of concentrated soda to about 100 ccm. (3½ fl. ozs.) of the excretion, warming gently for a short time, allowing to

cool, filtering (from phosphates, etc.), making decidedly but not too acid with a few drops of hydrochloric acid, and adding potassium-bismuth iodide solution. First of all a discolored amorphous precipitate of a compound with the nucleo-albumen of normal urine is formed; this contains no piperazine. The whole is warmed for a short time to 40° to 50°, whereby the precipitate aggregates, rapidly cooled and filtered. On energetically stirring with the glass rod, the bismuth-piperazine compound crystallizes out gradually, and falls as a fine pomegranate-red powder, the stellate crystalline form of which may be readily identified under the microscope.

The most valuable chemical property of piperazine is its power of forming a readily soluble compound with uric acid.* If brought together in cold, aqueous solution with uric acid it dissolves 12 times as much as will carbonate of lithium under the same conditions, and the piperazine urate formed is seven times more soluble in water at 17° C. than urate of lithium. One part of the latter requires 368 parts of water for solution, while one part of piperazine urate is taken up by 50 parts of water. Even when an excess of the acid is present only the readily soluble neutral salt is formed.

Medicinal Uses.—It was at first anticipated that piperazine would display nervine and stimulant properties similar to those ascribed to "spermine" (Brown-Sequard, Poehl and others), the active principle of which was believed to be a body of the same constitution. Physiological experiment and chemical investigation showed that this was not the case; the compound appeared to be practically inert, and certainly without powerful physiological effect (Kobert, Bock). Consideration of the behavior of the base with uric acid suggested its employment in the affections characteristic of the gouty diathesis. Earlier researches on the effect of the administration of piperazine upon metastasis was believed to indicate the fact that the amount of urea increased

*It is noteworthy that, according to Professor R. Kobert, *Cadaverine*, $C_5H_{14}N_2$—a ptomaine with some chemical relationship to piperazine—possesses the same property of forming a relatively readily soluble urate.

while that of the uric acid decreased (Vogt, Vigier and Gautrelot). This conclusion, however, was not confirmed by later observers. The compound was tried with fairly encouraging results in mental diseases (Umpfenbach, Peretti, Schultze), but by far the greater share of attention has been concentrated upon its uric acid solvent properties. It is very well borne without any ill results even when given for prolonged periods (Ebstein, Sprague and others), and exerts a marked solvent action upon concretions of urates and gouty tophi (Bardet). This latter property has been tested in the laboratory (Holtz) and practically evidenced in the clinical treatment of cases (Heubach and Kuh, Krakauer, Brik, Biesenthal and Schmidt). In 15 grain doses daily the use of piperazine in gout has been promptly followed by reduction of redness and swelling of the affected joints, while a general feeling of well-being set in ; very frequently the administration of the remedy is followed by a discharge of gravel. As a solvent for uric acid and urate concretions it is far superior to all known medicaments (Biesenthal & Schmidt); it should be tried in cases of rheumatic arthritis, where the diagnosis is difficult. Marked relief is afforded by the remedy in the pruritus of the uric acid diathesis due to the irritation of imperfect nitrogenous elimination (Disbrow).

Being without caustic action upon the mucous membrane solutions of piperazine may be directly introduced into the bladder in order to dissolve vesical stones, and by virtue of its solubility and non-irritating properties is suitable for local subcutaneous administration in gout. A solution (1 to 2 per cent.) in a mixture of water and spirit (1:4 respectively) has been recommended for topical application by means of the Priessnitz compress.

Piperazine is readily absorbed from the stomach and passes through the organism without suffering dissociation or resolution. Circulating with the blood unchanged, it is believed to reach the areas affected by gouty deposits in a condition in which it is readily able to neutralize and dissolve them and thus facilitate their removal from the body. Comparative experiments have also been made upon the diffusibility of piperazine, sodium and lithium urates, through

animal membrane, which established the superiority of the first named (Biesenthal and Schmidt).

A combination of phenocoll and piperazine in solution with plain or aërated water—15 grains of each per pint—is specially recommended as an effective and agreeable form of taking the remedy. In the proportion indicated it does not affect the taste of the water and has been successfully used in practice.

DERIVATIVES AND ALLIED COMPOUNDS.

By the action of *p*-chlornitrobenzol upon piperazine *β-nitrophenylpiperazine* melting at 129° is obtained. A dinitro-product is yielded if excess of the chlornitrobenzol be employed. *Diacetylpiperazine* ($C_4H_8N_2$. $2C_2H_3O$) is the product of the action of excess of acetic anhydride upon piperazine acetate under a return condenser; m. p. 138.5°. Other derivatives have also been obtained, but it does not seem intended to introduce them into medicine.

PYRIDINE.

C_5H_5N.

A liquid body formerly regarded as constitutionally analogous to chinoline, but recently stated to exhibit differences in behavior so important that the nitrogen atom is believed to occupy a different position in the molecules of the two compounds.

Preparation.—From bone-oil, by treatment with sulphuric acid, separation of the sulphonic compounds and decomposition with soda. The mixture of bases set free (pyridine, anilines, etc.) is carefully fractionated, the distillate treated with acid oxidizing agents (which attack only the aniline bases), neutralized with soda and fractionated again. Small quantities of very pure pyridine are obtained by distilling calcium nicotate with lime, thus :—

$$(C_5H_4NCOO)_2Ca + Ca(OH)_2 = 2\,CaCO_3 + {}_2C_5H_5N.$$

Calcium nicotate. Pyridine.

Physical and Chemical Properties.—Pure pyridine is a colorless liquid, with a peculiar empyreumatic odor and a pungent taste; specific gravity (at 0° C.) 0.9858; boiling

point 117° C. Miscible with water in all proportions, and considerably hygroscopic. Pyridine forms salts with acids by direct addition, like the alkaloids, of many of which, as known, it is regarded as the parent substance. It is distinguished from aniline bases in its power of resisting the action of oxidizing agents.

Pyridine should not be altered by exposure to light; it should not contain ammonia (as evidenced by the addition of phenolphtalein to the 10 per cent. aqueous solution), and two drachms of the same aqueous solution to which three drops of volumetric permanganate solution have been added should maintain the red color for at least an hour (absence of readily oxidizable compounds).

Medicinal Uses.—Internally pyridine has been given pure—3 to 4 drops three times a day—as a stimulant in cardiac diseases. Against diphtheria it has been locally applied, a 10 per cent. aqueous solution or a mixture of pyridine and peppermint oil being painted on the affected parts.

Pyridine bases are well known to occur in tobacco smoke, which has frequently proved beneficial in asthma; its use has therefore been recommended for the relief of asthmatic troubles (Germain Sée). From 1 to 1½ drachms are poured on a plate and placed in the room with the patients. In a temperature of 68° F. to 77° F. the above named quantity is evaporated in about an hour. It is said that after a few minutes of exposure to the pyridine atmosphere the remedy can be detected in the urine. The treatment was well-spoken of (Kelemen), but does not seem to have maintained its ground. In aqueous solution (1:300) 3 or 4 injections have been said to be sufficient to cure gonorrhœa (Rademacher), but this statement has not been confirmed by others (Wollenberg).

RESORCIN.

Synonym: METADIOXYBENZENE.

$C_6H_4(OH)_2$.

A compound primarily prepared in 1864 by Barth and Hlasiwetz from umbelliferous resins by fusing with potash.

Preparation.—By converting benzene into benzene disulphonic acid, neutralization with milk of lime, decomposition with soda, filtration (to remove the chalk formed), and evaporation to dryness. The product (sodium *m.*-benzenedisulphonate) is fused with caustic soda for eight or nine hours, the mixture allowed to cool, dissolved in boiling water, hydrochloric acid added, the boiling continued till all the sulphurous anhydride has escaped. On cooling the mass is filtered, the filrate extracted with ether, the latter evaporated off, and the residue heated to 275° C. (to remove the last traces of ether and water). The commercial product thus obtained is purified by distillation. The reaction between the sodium *m.*-benzenedisulphonate and sodium hydrate may be represented as follows :—

$$C_6H_4(SO_3Na)_2 + 2\,NaHO = 2\,SO_3Na_2 + C_6H_4(OH)_2.$$

Sod. *m*-benzenedisulphonate. *m*-dioxybenzene.

Physical and Chemical Properties.—Colorless or faintly yellowish tabular or columnar crystals, with a scarcely perceptible urinous odor, and an unpleasant sweetish pungent taste ; when pure and anhydrous it melts at 118° C. (100° to 111° C., Ph. G.) and boils at 276° C. It is readily and abundantly soluble in water (1:1 P. G.), alcohol (2:1 P.G.), and in ether, but scarcely at all so in cold benzene, chloroform and carbon bisulphide.

Heating to the melting point for a few minutes with an equal weight of phtalic anhydride and added to water the "fluorescein" formed gives the latter an intense yellowish-green fluorescence. One grain warmed with 2 grains of tartaric acid and 10 drops of sulphuric acid forms a dark carmine-red liquid.

Inorganic impurities are detected by combustion on platinum foil ; phenoloid bodies or acids by the odor and reaction with litmus paper—a feeble acidity should be allowed (Brenstein); and empyreumatic impurities by solution in 10 times the weight in water (to which they communicate a yellow tint). Imperfectly refined products are detected by their low melting point ; they can be purified by treatment with animal charcoal and crystallization.

Medicinal Uses.—Resorcin, as may be gathered from

the formula, is allied to phenol, differing in the substitution of a hydroxyl group for a hydrogen atom. It also closely resembles that compound in its physiological and medicinal effects, but is free from the eminently toxic action of the monohydroxyl benzene. It was early recommended for its antiseptic and antipyretic properties (Andeer) against nausea and vomiting, gastritis, (Menche, Andeer), and in asthma. The dose for internal use varies from 1 to 2 grains in sea-sickness, gastric affections, cholera infantum, etc., to 15 against asthma.

Externally resorcin has been used in diphtheria, especially as a 10 per cent. resorcin glycerole for topical application, with injections of a 1 per cent. aqueous solution in the nasal form. A majority of observers obtained excellent results (Andeer, Callias, Cattani, Ehrhardt, Leblond, Baudier and others) but a few voices have been raised against it (Nothnagel, Rossbach, Loebisch, Loeffler). Locally used, a 1 per cent. solution being painted on the throat, very satisfactory results are recorded in whooping-cough (Moncorvo, Bouchut, Callias, Mauriac, Andeer, Barlow, Guias). In ointment (5 to 10 or even 25 per cent.) resorcin has done good service in skin disease (Dreckmann), as also in the treatment of painful ulcers of the feet (Thoer). When solutions are used it is important to remember that weak solutions (1 to 3 per cent.) harden the skin, while stronger ones (10 to 50 per cent.) macerate and destroy it. Other forms in which resorcin has been used are wool and gauze (in general surgery), injections and sprays.

DERIVATIVES AND ALLIED COMPOUNDS.

Resopyrin is the name of a compound of resorcin and antipyrine obtained by the interaction of molecular proportions in solution (each in 3 parts of water); an abundant white precipitate is formed with some included oily drops. On violent agitation the oily mass increases and then suddenly solidifies to a hard white opaque body, resopyrin. From alcoholic solutions it can be obtained in fine rhombic, odorless crystals, insoluble in water, but taken up by ether (1 : 100), by chloroform (1 : 30) and by alcohol (1 : 5); solu-

tion in the latter menstruum is not precipitated by water. It differs chemically from resorcin by not giving a precipitate with lead subacetate, nor a blue color with ferric chloride. When gradually heated it separates into two layers, an oily and an aqueous. The physiological and therapeutical action of this body are still undetermined.

Thioresorcin, $C_6H_4(OS)_2$, is a yellowish-grey, tasteless powder, insoluble in water, and only sparingly taken up by alcohol and ether. Has been used as an iodoform subtitute for ulcers of the leg (Guttmann). Its application appears to be sometimes followed by unpleasant symptoms (Amon), though these may be traceable to admixture of resorcin.

Fluorescein, or resorcin-phtalein, $C_{20}H_{12}O_5$, occurs as dark-brown crytals, which form with ammonia a red solution, exhibiting a beautiful green fluorescence. Recommended for the diagnosis of corneal lesions, and detection of minute foreign bodies imbedded in that tissue. When an aqueous solution is dropped upon the cornea, those parts, however small, which are deprived of their epithelium are colored green, while foreign bodies are surrounded by a green ring (Straub). There seems to be some advantage in combining with the solution (10 grains to the ounce) one and a half times as much sodium bicarbonate (Randolph).

Hydroquinone, or paradioxybenzene, isomeric with resorcin, is prepared from aniline by oxidation with chromic acid mixture, and reduction of the quinone ($C_6H_4O_2$) formed by sulphurous acid. It is also a product of the splitting-up of arbutin by hydrolysis, thus:—

$$\underset{\text{Arbutin.}}{C_{12}H_{16}O_7} + H_2O = \underset{\text{Sugar.}}{C_6H_{12}O_6} + \underset{\text{Hydroquinone.}}{C_6H_6O_2}$$

Paradioxybenzene forms long colorless dimorphous crystals, melting at 169° C., difficultly soluble in cold water, readily so in hot water, in alcohol and in ether.

The compound has been employed as an antifermentative and antiseptic (Brieger, Lewin). In 1883 it acquired some reputation as an antipyretic (Silvestrini, Picchini, Traversa), the reduction of temperature taking place 30 to 40 minutes after the dose, 6 to 9 grains. Fresh solutions are free from caustic properties, and hence have been used sub-

cutaneously and as injections in gonorrhœa (1 to 2 per per cent. solution). The internal use of hydroquinone in typhoid has been suggested in doses of 3 to 8 grains.

As known hydroquinone is largely used in photography as a developer.

Pyrocatechin, or orthodioxybenzene, the third of this group of isomers, with the general formula $C_6H_4(OH)_2$, occurs as acicular crystals, soluble in water, alcohol, ether and hot toluol; m. p. 104° C., b. p. 240° to 245°. Aqueous solutions reduce silver salts in the cold and Fehling's solution on warming; if made alkaline they absorb oxygen rapidly and change to green in color and finally to black. Pyrocatechin has been tried therapeutically as an antipyretic (Brieger, Masing), but abandoned on account of its by-effects.

SACCHARIN.

Synonyms: Benzoyl-sulphonic imide; Gluside; Glucusimide.

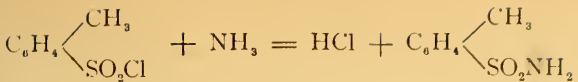
$$C_6H_4\begin{Bmatrix} CO \\ SO_2 \end{Bmatrix} NH$$

A derivative of the aromatic series, distinguished by its powerfully sweet taste.

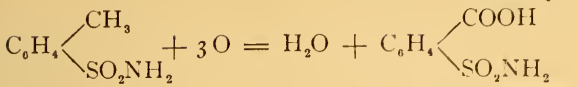
Preparation.—According to the patent specifications, by conversion of toluol into a sulphonic-acid compound, and of this into a sodium salt. By the action of phosphorus pentachloride the sodium salt is decomposed and a mixture of ortho and para toluol sulphochloride formed; the former isomeride is freed from the latter by cooling (when the para modification crystallizes out), and by the action of ammonia converted into orthotoluol-sulphamide. The next step is oxidation of the sulphamide into orthosulphaminbenzoic acid, which splits up into water and orthosulphaminbenzoic anhydride or benzoyl-sulphonic imide. The principle reactions are represented as under:—

1) $C_6H_4\begin{Bmatrix} CH_3 \\ SO_3H \end{Bmatrix} + PCl_5 = POCl_3 + HCl + C_6H_4\begin{Bmatrix} CH_3 \\ SO_2Cl \end{Bmatrix}$

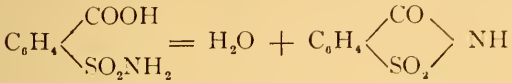
Toluolsulphonic acid. Toluolsulphochloride.



o.-Toluolsulphamide.



o.-Sulphaminbenzoic acid.



Saccharin.

Physical and Chemical Properties.—A white, uncertainly-crystalline powder, with an intensely sweet taste and a faint amygdaloid odor. Slightly soluble in cold water (1:400 at 15° C.), forming a feebly acid liquid; more soluble in alcohol (1:30) or glycerine; freely so in dilute ammonia, or in solution of sodium bicarbonate (evolving CO_2). According to the British Pharmacopœia Addendum, 1890, 100 parts of gluside mixed with water, warmed, neutralized with bicarbonate of soda, and evaporated to dryness, yield 113 parts of soluble gluside or saccharin. Probably in dissolving in water the acid is re-formed.

As evidence of identity the hepar reaction is officially adopted, and the absence of carbohydrates is ensured by providing that neither gluside nor soluble gluside shall be blackened when warmed with strong sulphuric acid.

Further proofs of purity are the absence of residue when heated on platinum foil, of a brown color when heated with potash lye (grape sugar), and of a red precipitate when warmed with Fehling's solution (natural sugars). Salicylic or benzoic acids, if present, are detected by the violet color produced on addition of ferric chloride to the ethereal filtrate, mixed with ten times its volume of water. Mannite is detected by the azure blue color produced when a solution of soluble saccharin so contaminated is exactly precipitated by cupric sulphate, filtered, sodium lye added and boiled.

Commercial saccharin seems to be far from a pure or simple substance; it contains about 50 per cent. of impurities, consisting of the isomeric (and less- or non-sweet) para com-

pound and of acid *o*-sulphobenzoate of potassium (Remsen and Burton, Dohome). The substance may be readily tested by treating with ether, which dissolves out the benzoyl sulphonic imide and leaves undissolved all foreign matter.

For the detection and estimation of saccharin in food stuffs of all kinds, and especially in cane sugar, various processes have been suggested. According to Reischauer, 4 ounces of the suspected material (when this is cane sugar) are treated for a few hours with 6 to 10 oz. of ether and filtered. If the sugar exhibit an alkaline reaction, instead of the solid substance, a concentrated aqueous solution feebly acidified with phosphoric acid should be shaken out with ether; in both cases the ether takes up the greater part of the saccharin contained in the sugar, which is left as a residue on evaporation and can be recognized by the taste, or in the following manner: The residue is melted gradually and carefully (otherwise violent explosion occurs) in a platinum capsule with a mixture of carbonate of soda and nitrate of potassium (6:1), and finally incinerated. The residue, dissolved in water, is tested for sulphates and the amount of sulphate of barium formed multiplied by 0.785 gives the weight of saccharin extracted; other compounds of sulphur possibly occurring in sugar are not taken up by the ether.

For the detection of saccharin in urine, C. Schmitt recommends that the liquid should be first tested for salicylic acid. If this be absent, 4 oz. of the strongly acidified liquid are shaken out three times with a mixture of equal parts of ether and petroleum ether, the extract mixed with soda solution and evaporated to dryness. The residue is heated for half-an-hour in a silver or porcelain capsule to 250° C., the mass dissolved in water acidified with sulphuric acid and shaken out with ether. The ethereal extract on evaporation of the solvent gives the ordinary reactions of salicylic acid (with ferric chloride for instance), produced in the decomposition of any saccharin present.

Beer is neutralized (about 2 pints being used) with sodium carbonate, evaporated to a syrupy consistence, and mixed by assiduous agitation with three or four times the volume of strong alcohol. After a few hours the mixture is filtered (the

residue being washed with alcohol), the filtrate distilled, the residue taken up with water, diluted to about four or five ounces, strongly acidified with phosphoric acid, and shaken out three times with ether, each agitation being continued at least an hour. The ethereal solution is distilled, the residue neutralized with sodium bicarbonate solution, filtered and evaporated to dryness on a watch. glass. The residue is recognized as saccharin either by the taste or by conversion into salicylic acid by heating with pure caustic soda to 250° to 270° C.

If salicylic acid be present in the beer, the ethereal residue, neutralized with soda, must be treated with mercuric nitrate, the precipitate (mercuric saccharinate) collected, washed, and dried by pressure between bibulous paper. It is then mixed, by melting, with excess of resorcin, a few drops of concentrated sulphuric acid are added, and the whole again warmed; the mass assumes various colors, froths and resinifies, while sulphur dioxide is given off. On cooling the mass dissolved in a little water gives with excess of caustic potash a deep brown liquid, with a green fluorescence which is more pronounced if a few drops be removed and diluted with more water.

A great deal of discussion has centred around the question whether saccharin is injurious to the animal organism or not, but it may be regarded as now established that it has no effect upon the system whatever. The compound passes through the body unchanged, and appears neither in the saliva nor the milk but is entirely excreted by the urine. It seems to be without marked effect even upon the action of the animal ferments and upon micro-organisms in general, though the activity of *Saccharomyces cerivisiæ* was prejudiced by the presence of a quantity bearing the proportion to the yeast taken of 1 : 20 (Kornauth). Given in large doses continually to animals—which do not exhibit any disinclination to take the substance—saccharin had no appreciable effect upon the organism or upon the processes of nutrition.

Medicinal Uses.—The chief uses of saccharin in medicine are as a sweetening agent for the food of diabetics and as a general flavoring and corrective. For the former purpose its

property of passing though the organism unchanged is believed to make it specially applicable. It has also been found to have a well-marked antiseptic action and has proved beneficial in the treatment of cystitis and urethral inflammation (Little, Colquhoun). By far the larger proportion seems to be used in sweetening various foods, confectionery, &c., and it seems to be generally unobjectionable for such purposes; as however, it is not a food it cannot substitute sugar in all cases, and hence the necessity for the many processes for its detection.

An excellent and agreeable mouth wash is made by dissolving 10 grains each of saccharin and sodium bicarbonate in about 10 fluid drachms of spirit (warming gently to facilitate combination and the escape of carbon dioxide), adding 10 to 20 grains of salicylic acid, and making up to 1 fluid ounce with spirit. One teaspoonful of this spirituous solution with 4 fluid ounces of water forms an effective solution for the purpose indicated.

For use in pharmacy various elixirs, syrups, etc., are prepared, and compounds of saccharin with certain bitter alkaloids and principles (*e. g.* quinine) have also been manufactured and employed in medicine.

DERIVATIVES AND ALLIED COMPOUND.

Paraphenetol-carbamide, $C_6H_4(OC_2H_5)NH.CONH_2$, is another synthetical compound which possesses an exceedingly sweet taste. It is obtained by the action of ammonia upon an intermediate body produced by the action of one molecule of carbon oxychloride upon two molecules of *p*-phenetidin. When pure the compound occurs in the form of colorless needles, melting at 160° C. It is said to be free from any injurious action upon the human organism.

SALICYLAMIDE.

$$C_6H_4\begin{cases}OH\\CONH_2\end{cases}$$

One of a large group of amidogen compounds, some members of which are well known in medicine (chloralamide, chloralurethane, urethane).

Preparation.—Preferably by the action of concentrated ammonia upon crude methyl salicylate as obtainable in the form of wintergreen oil. When these stand in contact (cold) for some days the liquid assumes a deep reddish-brown color and brownish crystals begin to separate; impurities are removed from these by recrystallisation and treatment with animal charcoal. It may also be obtained by the action of heat upon ammonium salicylate.

Physical and Chemical Properties.—When pure, salicylamide occurs in perfectly colorless, thin, transparent plates, melting at 142° C., soluble in alcohol, ether, chloroform and 250 parts of water (salicylic acid 1 : 500). It is quite tasteless, but produces a feeling of grittiness between the teeth. Salicylamide prevents the putrefaction of wine and other organic liquids for months.

Medicinal Uses.—This amide derivative of salicylic acid seems to closely resemble the parent substance in its therapeutical properties, but has the advantages of being tasteless and more soluble. It also acts more promptly, and in smaller doses is a more powerful analgesic and safer (Nesbitt). Salicylamide is excreted in the urine chiefly as salicyluric acid; as indicated above it has decided germicidal properties and retards diastatic and peptic change, though to a less extent than salicylic acid. In 3 to 5 grain doses (up to 15 grains a day) it was given successfully in ovarian pain, neuralgia, chronic rheumatism and follicular amygdalitis (*Ibid*).

SALOL.

Synonym : Phenyl Salicylate.

$$C_6H_4 \begin{cases} OH \\ COOC_6H_5 \end{cases}$$

One of the first organic salicylates, introduced into medicine in 1886.

Preparation.—Molecular proportions of salicylate of soda and sodium-phenol are caused to react by prolonged heating in the presence of phosphoric oxychloride. The reaction may be expressed as follows:—

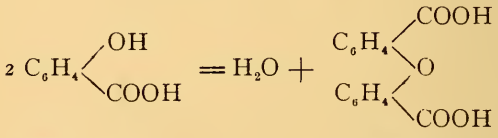
$$2\ C_6H_5ONa + 2\ C_6H_4OHCOONa + POCl_3 =$$
Sodium phenol. Sodium salicylate.

$$3\ NaCl + NaPO_3 + 2\ C_6H_4OHCOOC_6H_5.$$
Sod. phosphite. Salol.

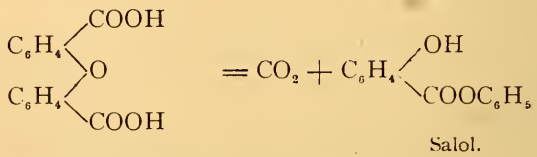
The product is treated with water, washed till practically free from chloride and phosphate, and finally crystallized from alcohol. It may also be obtained by leading phosgen gas into a warmed intimate mixture of salicylate of sodium and sodium-phenol. The reaction is quite similar to the above, except that the secondary products are sodium chloride and carbon dioxide.

A later patented process consisted in heating pure or even crude salicylic acid in a bath to 220° to 230° C. The vessel containing the acid has a narrow neck reaching so far out of the bath that at the temperature named the water vapors formed do not condense and fall back into the vessel but can be conducted away. If the neck be not heated much above the temperature necessary to ensure this only steam and carbon dioxide escape. Air is excluded by filling the vessel with an indifferent gas (*e. g.* CO_2) and leading in a feeble stream of the same during the heating.

The most probable explanation of the reaction is that water is first split off, forming an anhydride-like body, and that this gives up carbon dioxide, and, intermolecularly, or with undecomposed salicylic acid, condenses to salol. For instance,



Salicylic acid. Anhydride.



Salol.

Physical and Chemical Properties.—A white crystalline powder, or transparent tabular crystals, with a faint aromatic

odor, practically tasteless, being insoluble in water. It is taken up by 10 parts of alcohol, or less than its own weight of ether; an alcoholic solution forms with water a kind of emulsion. It is also considerably soluble in copaiba balsam, in sandalwood oil, in turpentine, and in fatty or mineral oils. Melting point 42° to 43° C.; heated on platinum foil it burns away without residue.

In a solution of ferric chloride an alcoholic solution of salol produces only a turbidity but no color; on the other hand, ferric chloride produces in an alcoholic solution of salol the characteristic violet color of phenol. Bromine water precipitates monobromsalol. The ether is split up by warming with the fixed alkalies into salicylate and alkali-phenol.

Free mineral acid (phosphoric) is detected by blue litmus paper. Free phenol or salicylic acid is evidenced by the behavior of an alcoholic solution with three times the volume of water, to which previously a drop or two of ferric chloride has been added; a permanent violet color is produced if these impurities be present.

Medicinal Uses.—Salol was prepared and introduced into medicine after physiological examination (Nencki, Sahli), as the result of researches with the view of discovering a compound of salicylic acid which should be free from the disadvantages of most salicylates. The first experiments showed that salol possessed antiseptic, antipyretic and antirheumatic properties, and it was especially recommended in rheumatism. At the same time it was found that the remedy being insoluble passes unabsorbed and unchanged through the stomach and is only decomposed (into salicylic acid and phenol compounds) by the alkaline juices of the intestine. To this intestinal dissociation its particular virtues are largely due, as by its means local antisepsis becomes possible in such affections as acute diarrhœa, dysentery, cholera, etc. (Goelet, Cahall, Moncorvo, Nicholson, Löwenthal, Hüppe).

Being entirely excreted with the urine—which exhibits the characteristic dark color of phenol-urine—in the form of salicyluric acid and phenol compounds of marked antiseptic powers, salol has been administered internally in the treatment of affections of the bladder and urethra, *e.g.* catheter

fever, fermentation of urine in the bladder, and especially gonorrhœa (Mumford, Lane). For the latter purpose it may be combined with copaiba or sandal-wood oil, in which it dissolves without difficulty. Good results are recorded from its use in gonorrhœal arthritis (Vernon Jones).

Some discussion has arisen as to the safety or otherwise of salol when given internally. Many authorities maintain that it may be given in large doses without risk (Georgi, Sahli, v. Jaksch), while others report symptoms of poisoning and even deaths after comparatively small doses (Hesselbach, Chlapowski). The remedy has, however, been very widely used without such untoward effects, and it seems likely that the cause of the toxic symptoms in the few cases alluded to should have been looked for elsewhere.

More recent additions to the therapeutics of salol have elucidated its value internally in pharyngeal inflammations (Gouguenheim, Caport), and combined with terpin hydrate (ana 3 grains) in bronchitis, catarrhal fever and colds generally (Cohen). It has also been tried in the treatment of leprosy and yellow fever.

The dose of salol as powder is 1 to 2 drachms daily in divided portions; in the diarrhœa and other intestinal troubles of children 2 to 3 grains may be given every three hours. In cholera, 8 grains salol has been prescribed in combination with 3 grains bismuth salicylate every three hours (Hüppe).

Externally, the compound is used as an antiseptic and deodorant, similarly to iodoform, in the form of gauze, dusting powder (1 : 1 to 3 French chalk or starch), collodion (4 : 4 ether and 30 collodion), and of 5 to 10 per cent. alcoholic solution (with twenty volumes of water for gargling in angina, etc). In ointments and compound powders it has been found the best remedy against impetigo, eczema, and sycosis (Saalfeld), and has also done good service as an insufflation in the treatment of ozæna.

A powder consisting of salol, 15 grains, salicylic acid, 3 grains, tannic acid, 2 grains, and powdered boric acid, 1 grain, has been recommended as an insufflation into each nostril for the aborting of acute coryza (Capitan). Some care appears, however, to be necessary in using it as it is not

altogether free from caustic action upon the nasal mucous membrane if snuffed in too large quantities and too frequently. The treatment should not be continued more than a few hours at most.

Spirituous solutions (about 5 per cent.) are employed with various flavoring agents for the preparation of mouth-washes and dentifrices, while it is largely used in the preparation of other toilet preprrations, *e. g.*, powders and soaps.

DERIVATIVES AND ALLIED COMPOUNDS.

Salol-camphor is made by mixing 3 parts of salol with 2 parts of powdered camphor, heating gradually to complete fusion and filtering; the product is preserved in yellow hermetically sealed bottles. It is a colorless liquid of oleaginous character, insoluble in water, freely soluble in ether, chloroform and oils; under the influence of light and air it readily decomposed. Recommended in the treatment of purulent inflammation of the middle ear, pledgets of cotton-wool soaked in the camphorated salol being introduced into the external meatus previously thoroughly cleansed. Repeated every twelve or twenty-four hours, syringing with boric lotion in the intervals, this method cures most forms of suppurative otitis (Pégou).

Salophen, chemically described as *p* amidophenol salicylate, may be looked upon as salol in which an atom of hydrogen in the phenyl group is replaced by the monivalent group ($NHCOCH_3$), its formula being

$$C_6H_4{<}^{OH}_{COOC_6H_4N{<}^{H}_{COCH_3}}$$

It contains the equivalent of 50.9 per cent. of salicylic acid, and occurs as minute white crystalline scales, almost entirely insoluble in water, free from odor and taste. Alkali, alcohol and ether take it up freely, and the alcoholic solution is colored violet by ferric chloride; salophen melts at 187° to 188° C.

Exhaustive pharmacological experiments with salophen showed that in the organism it is split up and excreted as salicyluric acid and acetyl-*p*-amidophenol compounds; it is comparatively little poisonous (Siebel). Therapeutically it has been pronouuced useful in acute rheumatic arthritis, in doses of 1 to 1½ drachms *pro die* (Guttmann).

SOZOIODOL.

Synonym: Diiodparaphenolsulphonic Acid.

$C_6H_2I_2OHSO_3H$.

A crystalline monobasic acid, introduced in 1887 as an antiseptic; it contains 52.8 per cent. of iodine and 7 per cent. of sulphur.

Preparation.—By the interaction of potassium paraphenolsulphonate, dissolved in dilute hydrochloric acid, and a solution of potassium iodate and iodide, in molecular proportions (or of iodine chloride). Finely-divided iodine first separates, and then again re-dissolves. After a short time long white needles come out of solution, which are the potassium salt of sozoiodol.

Physical and Chemical Properties.—Sozoiodol crystallizes from water in acicular prisms, which lose their three molecules of water of crystallization when exposed over sulphuric acid. It is readily soluble in water, in alcohol and in glycerine.

The presence of iodide or of chloride is detected by the precipitate formed when argentic nitrate is added to a solution of sozoiodol in nitric acid, and of sulphate by the insoluble precipitate formed on the addition of barium chloride. (Barium sozoiodol is soluble in boiling water).

Medicinal Uses.—Sozoiodol was put forward as combining in itself the antiseptic and general therapeutical virtues of iodine and carbolic acid; at the same time it could not manifest the poisonous properties of the latter as the phenol was present in the form of the harmless compound carbolsulphonic acid. In the organism it does not appear to be split up but is resolved into and excreted as an organic compound of uncertain nature, which has no irritating influence upon the kidneys (Langgaard and Buffalini).

In 2 per cent. solution both sozoiodol and sozoiodol sodium entirely prevent the development of pus cocci. Its absolute freedom from odor, its solubility and stability under normal conditions constituted its chief claims of preference over other iodine compounds. It has been used in all cases where iodoform is considered indicated.

Either the acid itself, or its preparations, has been employed in skin diseases (Lassar, Schwimmer, J. Koch), in rhinopharyngology (Fritsche, Seifert, Herzog, Stern), in gynæcology (Nitschmann), and in general surgery, burns, etc. (Thomann, Ostermayer). In venereal diseases, gastric affections, and rheumatism its successful use has been also reported, while further it has been recommended in dental surgery and in veterinary practice.

The forms in which the compound is applied resemble those adopted generally for iodoform and its substitutes, *e. g.* dusting powder (5—10—20 per cent. with French chalk) collodion, solutions, gauze, etc.

DERIVATIVES AND ALLIED COMPOUNDS.

The salts of iodophenolsulphonic acid, or at least the most important described below, have been more employed than the parent substance.

Potassium and *sodium sozoiodol*, $C_6H_2I_2(OH)SO_3K$ (or Na), form colorless well defined prisms, soluble in water—the potassium compound in 50, the sodium in 14 parts. The solutions are acid, and give a bluish violet with ferric chloride. Fuming nitric acid displaces iodine, picric acid being simultaneously formed; barium chloride produces a precipitate, soluble on boiling. The aqueous solutions gradually darken under the influence of light.

The sodium salt has yielded better results in idiopathic ulcerative processes than in those of syphilis. In vesical affections the bladder is irrigated with a 1 per cent. solution, and the same application is recommended in catarrhal conditions of the nasal mucous membrane.

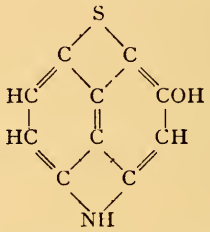
Zinc sozoiodol crystallizes in colorless needles with six molecules of water; it is soluble in water (1:20) and in alcohol. In ½ per cent. solution this salt has done good service in acute and chronic blennorrhœas and in a few cases of catarrhal inflammations of the nasal and pharyngeal mucous membranes, either as a powder with 10 to 15 parts of French chalk, as paint or mouth wash.

Mercury sozoiodol, $[C_6H_2I_2(OH)SO_3]_2Hg$, is a lemon-yellow subtile powder, scarcely soluble in water (1:500), but much

more readily in sodium chloride. In 10 per cent. solution it appears to have a strongly irritant action. "With respect to its curative value this preparation is superior in certainty of effect to all other sozoiodol preparations" (Schwimmer). It has been chiefly used in the specific treatment of syphilis, locally and subcutaneously, as combining the freedom from local effects of soluble mercurials with the prolonged and energetic action of the insoluble. Dose, 1 grain in the gluteal region.

SULPHAMINOL.

Synonym : THIOXYDIPHENYLAMINE.



Preparation.—By the action of sulphur "in a suitable manner" upon the salts of *m*-oxydiphenylamine dissolved in water.

Physical and Chemical Properties.—Sulphaminol is a pale yellow powder, free from odor and from taste ; readily soluble in alkalies, more difficultly so in alkaline carbonates, quite insoluble in water. It is taken up by alcohol as well as by glacial acetic acid ; the solutions are colored pale yellow. When subjected to the action of heat it turns brown, and melts at about 155° C.

Medicinal Uses.—Pharmacological investigations have shown that thioxydiphenylamine is perfectly harmless, both to animals and to human beings (Kobert, Wojtaszek); when taken internally it is split up in the organism into oxydiphenylamine and sulphuric acid compounds. Sulphaminol possesses marked antiseptic properties, which render it suitable for application to the same purposes as iodoform. It has been successfully employed in pharyngeal tuberculosis, and further for the so-called dry treatment of suppurative

processes of the jaw. The offensive odor of the latter is only to be overcome by the application of iodoform or of sulphaminol (Moritz Schmidt). In the form of dusting powder it produces strikingly rapid and favorable results in rhinolaryngology (Robertson), in wounds, ulcers of the feet and bed-sores; has also proved beneficial internally against cystitis (Rabow). The single dose amounts to 4 grains in powder, the daily dose to 15 grains. In another case of cystitis and soft venereal ulcer no appreciable effects were produced by the employment of sulphaminol (Wojtaszek). It has been specially recommended for curing the so-called "putrid-brood" of bees, being several times applied in powder.

DERIVATIVES AND ALLIED COMPOUNDS.

Under the names *Sulphaminol-menthol*, *S.-creasote*, *S.-guaiacol*, *S. eucalyptol*, solutions of the compound in the different liquids named have been introduced into commerce, and brought under the notice of the medical world, especially for use in rhinolaryngology and laryngeal tuberculosis.

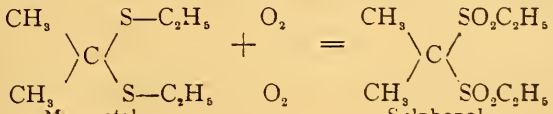
SULPHONAL.

Synonym: DIETHYLSULPHON-DIMETHYL-METHANE.

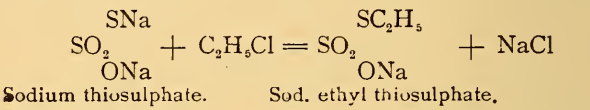
$$(CH_3)_2\,C\,(SO_2C_2H_5)_2.$$

A synthetical hypnotic, which has been admitted to a place in the official materia medica of several European countries.

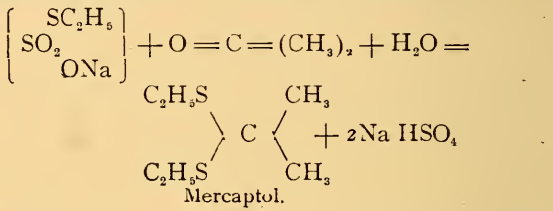
Preparation.—By the interaction of anhydrous mercaptan, and anhydrous acetone in the presence of a stream of dry hydrochloric acid gas. The liquid gradually becomes turbid and separates into two layers, of which the upper is mercaptol (dithioethyldimethylmethane $[CH_3]_2C[S\text{-}C_2H_5]_2$), the lower dilute hydrochloric acid (the water is a product of the reaction). The mercaptol is separated, washed, and oxidized by potassium permanganate, according to the following equation:—



It is also manufactured by the action of ethyl chloride or bromide on sodium thiosulphate, conversion of the resultant sodium ethyl thiosulphate into ethyl mercaptan and acid sulphate of sodium by the action of water. As this conversion takes place in the presence of alcoholic hydrochloric acid solution and acetone, the ethyl mercaptan is condensed *in statu nascendi* to mercaptol, which is oxidized as above described. The reactions may be represented as under :—



Sodium thiosulphate. Sod. ethyl thiosulphate.



Mercaptol.

The third stage is the oxidation of mercaptol to sulphonal, already illustrated.

Physical and Chemical Properties.—Colorless, inodorous, pratically tasteless, prismatic crystals, melting at 125° to 126° C. (B. P. Add. 125.5° C.). Soluble in 15 parts of boiling water, and in about 450 parts of that solvent cold; also in cold rectified spirit (B. P. Add. in about 50 fluid parts), and freely in boiling alcohol; soluble in ether (1:135 at 15°).

Sulphonal is a very stable body, being unaffected by concentrated acids, alkalies, or oxidizing agents, either in the cold or when warm. Chlorine and bromine also are without effect even when warmed. To this stability must be ascribed the lack of a characteristic reaction for the compound.

Officially, sulphonal must burn away without residue when ignited with free access of air. The test of Vulpius, according to which the repulsive odor of mercaptan is evolved when sulphonal is heated with potassium cyanide, is recognized in the Pharmacopœia, and it is added further,

that "when to the solution of the product in water excess of hydrochloric acid and a few drops of solution of perchloride of iron are added a reddish color is developed." This color is due to the formation of ferric thiocyanide. The same effect may be produced by heating sulphonal with gallic or pyrogallic acid, or with wood charcoal. The reaction is not peculiar to sulphonal, but it is produced by the whole classes of sulphones and disulphones, and by most mercaptan derivatives.

Further tests of the purity of the compound are that the solutions must be neutral and unaffected by barium or silver nitrate. Two ounces of a hot 2 per cent. solution must not immediately decolorize 6 drops of volumetric potassium permanganate solution.

The urine of patients who are taking considerable doses of sulphonal assumes a peculiar reddish-brown color, due to the presence of hæmatoporphyrin. This substance is best detected by observing the spectroscopic behavior of the solution in hydrochloric acid and ammoniacal solution; or the color may be precipitated by alkaline barium chloride solution, and the solutions obtained by treatment of the precipitate with alcohol containing hydrochloric acid spectroscopically examined (Salkowski).

Medicinal Uses.—Sulphonal was introduced in 1888 as a hypnotic which induced quiet and sound sleep, from which the patient awakened refreshed and free from any after-effects; blood pressure was not affected nor the blood itself, nor the digestive tract (Kast, Rabbas, Salgo, Rosin), and it was given by a long list of observers in mental diseases, in trismus, in nervous sleeplessness, and insomnia from pain and cough, etc. (Cramer, Oestreicher, Schwalbe, Fraenkel, Ott, Matthes, Ruscheweyn, Kronfeld, Löwenthal, Conolly, Norman, Mahon, Berenyi and many others). It was not long, however, before cases of unpleasant after-effects, poisoning symptoms, and even fatal issues after the administration of sulphonal began to multiply. Indictments against the remedy were brought by a number of observers (Schotten, Joachim, Garnier, Knoblauch, Vorster, Knaggs, Montzel), some of which characterized it as less a remedy than a

poison! Opinions and experience are, however, far from unanimous on the point.

Two propositions have been made which are claimed to increase the value of sulphonal as a hypnotic. One is to combine each dose (15 grains) with ½ to 1 grain of codeine (Svetlin), and the other is to dissolve the remedy in boiling water, add carefully just sufficient cold water to make the draught potable (or allow to cool sufficiently) and take immediately before bed-time. The action is more prompt, the sleep sounder, and after-effects (drowsiness, etc.) more rare (Stewart).

The dose of sulphonal is from 15 to 40 grains, and it may be taken in powder (wafers), substance, or in solution as described in the preceding paragraph. In 8 grain doses it has been prescribed against the night sweats of consumptives.

DERIVATIVES AND ALLIED COMPOUNDS.

Trional, $C_2H_5CH_3 - C - (SO_2C_2H_5)_2$, differs from sulphonal (as can be seen by comparing the formulas) only in the substitution of an ethyl for a methyl group, so that its systematic name is diethylsulphonmethylethylmethane. It forms lustrous, tabular, bitter crystals, melting at 76°C., requiring 320 parts of cold water for solution, but readily soluble in alcohol and in ether. This compound was expected to be a more powerful hypnotic than sulphonal, from the physiological experiments performed on animals; but Barth and Rumpel found that though evidently indicated in certain nervous diseases where sulphonal did not answer, the dose had to be quite as large (60 grains daily). It seemed to be less liable to produce ill-effects than sulphonal. The same is said to be true of the closely allied

Tetronal, $(C_2H_5)_2 - C - (SO_2C_2H_5)_2$, or diethylsulphondiethylmethane, which occurs in lustrous tabular crystals and plates, melting at 85°C. It is soluble in 450 parts of cold water, readily so in alcohol, and fairly in ether. The taste is camphoraceous and bitter. The name, of course, like "trional," which it physiologically and therapeutically resembles, has reference to the number of ethyl groups present.

Comparative experiments with these two allied compounds tend to show that, in general, trional is more active than tetronal, while at the same time the latter not unfrequently produces vomiting. Further, trional has extraordinarily few unpleasant by-effects (Schultze). The dose adopted is 30 grains two or three times a day.

THALLINE.

Synonym: TETRAHYDROPARACHINANISOL.

$C_9H_{10}N(OCH_3)$.

A liquid base, first prepared in 1885 by Skraup, who also effected the synthesis of chinoline.

Preparation.—According to the patent specifications, from parachinanisol, obtained by heating together paraamidoanisol and acrolein (= glycerine + sulphuric acid) in the presence of an oxidizing agent (paranitroanisol). By reducing agents parachinanisol takes up four hydrogen atoms, forming the base thalline. These two reactions may be represented as follows:—

$$\underset{\text{Paraamidoanisol.}}{C_6H_4NH_2OCH_3} + O + \underset{\text{Acrolein.}}{CH_2CHCHO} = \underset{\text{Parachinanisol.}}{C_9H_6N(OCH_3)} + 2\,H_2O$$

$$C_9H_6N(OCH_3) + 4\,H = \underset{\text{Tetrahydroparachinanisol.}}{C_9H_{10}N(OCH_3)}.$$

Physical and Chemical Properties.—At ordinary temperatures thalline is an oily liquid, solidifying when cooled to yellowish crystals. It has a strong odor, resembling cumarin, and forms well defined salts with acids.

Oxidizing agents (the halogens, the nitrates of silver and mercury, chromic acid, ferric chloride, etc.) produce an intense emerald green color, hence the name (*θάλλος* a green twig.)—Ferric chloride produces the color (which is not affected by addition of a drop or two of pure concentrated sulphuric acid) in very dilute solution (1:100000). Sodium thiosulphate changes the green tint into violet and then into wine-red, oxalic acid at ordinary temperatures into pale yellow, deepening into saffron on heating.

Medicinal Uses.—The base thalline itself is not suitable for use in medicine, and of the possible salts only the sulphate and tartrate have been used.

Thalline sulphate is a yellowish white crystalline powder, with a cumarin-like odor, and a taste described as at once acid, saline, bitter and spicy. Soluble in seven parts of cold or 0.5 part of boiling water; also in alcohol (1:100), difficultly so in chloroform and practically insoluble in ether. The aqueous solutions are acid, and when exposed to light gradually darken; by iodine solution they are precipitated brown, by tannin acid white, and by Nessler's reagent lemon yellow. Like the base itself this salt in 1 per cent. solution is colored emerald green by ferric chloride. When heated over 100° C. thalline sulphate melts, and if the temperature be raised it decomposes, burning away (if pure) without residue.

Thalline tartrate occurs as a yellowish-white crystalline powder, with an odor reminding of anise and cumarin; soluble in water (1:10), slightly so in alcohol, and practically insoluble in ether and in chloroform. In general it behaves like the sulphate, but is distinguished by giving no precipitate with barium nitrate.

Both these salts were at first given internally (doses of 2 to 8 grains) in aqueous solutions as antipyretics, and used externally as antiseptics, especially against gonorrhœa in the form of injections and bougies. Physiological experiments have not encouraged the internal use of thalline compounds; they are poisons for the red blood corpuscles and for the nervous system (Robin, Brouardel, Loye, Weinstein, Karst).

As an injection an aqueous solution is recommended, containing 4 to 8 grains to the ounce, or a compound solution of thalline sulphate (2 to 5 per cent.) with tannin (0.2 to 0.5 per cent.) and silver nitrate (0.02 to 0.05). Towards the end of the treatment antrophores are employed containing 2 per cent. of thalline, or bougies of the same strength made up with cacao-butter.

THIOL.

Preparation.—Brown-colored paraffin or gas oils of specific gravity 0.890 to 0.900 are treated with sulphur at high temperatures; the unsaturated hydrocarbons, which are alone attacked by the sulphur, are extracted by suitable solvents

from admixture with saturated hydrocarbons. By the action of concentrated sulphuric acid, under artificial cooling, products, soluble in water, are obtained. When the action of sulphuric acid is complete, pieces of ice are added to the mixture; thiol separates and is purified from acid and other impurities including a peculiar odorous principle. It is then evaporated (in vacuo) to a thin extract (thiolum liquidum) or to complete dryness (thiolum siccum).

Physical and Chemical Properties.—Liquid thiol is a thin brownish-black neutral extract, of specific gravity 1.080 to 1.082 at 15° C., with a feeble bituminous odor reminding of birch oil; it forms clear mixtures with water, especially if glycerine be added, but is only partly soluble in alcohol and ether. Aqueous solutions, which froth abundantly when shaken, are unaffected by addition of alcohol (or by subsequent addition of dilute nitric acid), but soda, dilute acids, or metallic salts precipitate them.

When evaporated to dryness thiolum liquidum yields 40 per cent. of residue (thiolum siccum), which when further heated on platinum foil burns away with a sooty flame leaving no residue (absence of fixed alkalies). The filtrate from aqueous solutions which have been completely precipitated with nitric acid should not be rendered turbid by addition of silver nitrate (chlorine), and only assume an opalescence on the addition of barium nitrate. Petroleum ether should extract no saturated hydrocarbons from aqueous solutions. Negative results should be yielded on testing for arsenic (derived from the sulphuric acid employed) in the ash obtained by incineration with a mixture of soda and nitre.

Medicinal Uses.—Thiol was introduced into materia medica in 1888 as an addition to the armament of the dermatologist against the many forms of skin disease which come under treatment.

It must be included among the so-called "reducing agents" employed in dermatology, but is preferable to many of them in its relative freedom from odor and staining properties; thiol spots are readily removed from textile fabrics (Schwimmer).

The literature of thiol contains reports of its successful use in eczema, acne, sycosis, erythema, erysipelas, lymphangoitis, and generally in (a) eczematous affections, (b) acute moist inflammatory processes of the skin and subadjacent tissues, (c) chilblains and periphlebitis, (d) acute infiltration of joints, œdema, and (e) contusions and subcutaneous hæmorrhage (Reeps, Buzzi, Neisser, Bidder, Schwimmer, Stepp). It has also been employed in a few chronic skin affections, in the ulcerous processes of syphilis, scrophulosis, lupus, in rheumatism (Schwimmer, Bidder), and in gynæcology. In the latter department of medicine it has done good service in the treatment of pelvic exudations, endometritis, etc. (Gottschalk).

Thiol may be applied as powder, collodion (5 per cent. of powder), aqueous or glycerine solutions (10 to 50 per cent.), ointment (10 per cent. of the liquid), soap, plaster, lanoliniment, gelatine, etc. Internally it is given dissolved in wine (1 per cent.) as chocolate (1 to 2 per cent.), and, in pills (1½ grains of the liquid each).

DERIVATIVES AND ALLIED COMPOUNDS.

Tumenol (from bi*tumen*) is a somewhat allied preparation obtained from mineral oil—freed from creasotes and acids (by soda) and from bases and pyrroloid bodies (by 70 per cent. sulphuric acid)—by the direct action of concentrated or of fuming sulphuric acid, without previous sulphuration. The product is washed free from excess of acid and forms crude tumenol.

Tumenol "venale" is a mixture of sulphones and sulphonic acids, occuring as a dark-colored acid syrup; the separated sulphones (extracted by ether from the soda-neutralized mixture) are introduced as "tumenol oil," a dark-yellow thick liquid, insoluble in water but readily soluble in ether and benzene, and taken up by the aqueous solutions of tumenol sulphonic acid. The latter is also prepared in a separate form as a dark-colored powder, with a peculiar feebly bitter taste.

Tumenol is to be used in (1) eczema, and (2) itching of all kinds (Neisser). It does not appear to determine the absorption

of exudations. Internally it has not exhibited any functional disturbances.

Externally it can be applied as tincture (10 per cent. in ether, spir. vini rect. and water or glycerine ana), ointment, paste, plaster, dusting powder, etc. A 2 to 5 per cent. solution of the powder may be applied with compresses locally. The tumenol oil has been painted on the diseased surfaces undiluted.

URETHANE.

Synonym : Ethyl-urethane.

$$CO\begin{cases} NH_2 \\ OC_2H_5 \end{cases}$$

One of a series of compounds which may be regarded chemically as esters of carbaminic acid.

Preparation.—By the interaction of nitrate of urea and ethyl alcohol at 120° to 130° C., extraction of the resultant urethane by ether and recrystallization.

$$\underset{\text{Urea nitrate.}}{CO<^{NH_2HNO_3}_{NH_2}} + \underset{\text{Alcohol.}}{HOC_2H_5} = NH_4NO_3 + CO<^{NH_2}_{OC_2H_5}$$

Physical and Chemical Properties.—Colorless, columnar, or tabular crystals, odorless, and with a nitre-like taste. Readily soluble in water and in most media; the solutions are neutral. Melting point 47° to 50° C.; boils between 170° and 180° C. almost without decomposition, giving off vapors which burn with a blue flame.

Urethane yields carbon dioxide when warmed with sulphuric acid (alcohol and ammonium hydrogen sulphate being also formed), and ammonia (as well as alcohol and potassium carbonate) with caustic potash. If 6 grains are dissolved in a drachm of water, 12 grains of dried sodium carbonate with a few granules of iodine added, and the whole gently warmed, iodoform separates on cooling.

Inorganic impurities are detected by heating on platinum foil; its entire volatility also serves to distinguish it from nitre. Urea is detected, if present, by the fact that in cold aqueous

solution it gives a white precipitate with nitric acid, oxalic acid, or mercuric nitrate.

Medicinal Uses.—Having been experimentally investigated as a hypnotic (Kobert and Schmiedeberg) urethane was introduced into medicine in 1885 (v. Jaksch). It was given as a sedative in mental diseases (Otto, König), and for the production of a quiet natural sleep in various cases (Riegel). It appears to produce no appreciable by- or after-affects, and being readily administered with the addition of any correctives is specially suitable for administration to children (Ewald). Good results have been yielded by it in tetanus following on injuries (Maresti), and like some others of the same class of remedies it has been credited with antidotal properties for the convulsive poisons (Anrep).

The dose of urethane is from 15 to 45 grains, in aqueous solution with correctives; subcutaneously it has been given in doses of 4 grains (Rottenbicher).

DERIVATIVES AND ALLIED COMPOUNDS.

Somnal. Under this name a solution of chloral hydrate and urethane in alcohol was introduced and employed to some extent as a hypnotic (Senator, Krafft-Ebing, Eulenberg, Langenbuch, Brandenberg and others), but seems now to have been entirely abandoned so far as any general use goes.

Uralium or *Chloral-urethane.* Chloral at ordinary temperatures or melted chloral hydrate dissolves urethane; if to such a solution concentrated hydrochloric acid be added it solidifies within twenty-four hours to a mass insoluble in water. This is then treated with concentrated sulphuric acid and washed with water, by which an oil results which subsequently crystallizes. The product ($CCl_3CH : OH.NHCO_2C_2H_5$) is insoluble in cold and decomposed by boiling water; it is abundantly taken up by alcohol and ether, and re-precipitated by water; melting point 103° C. Strongly recommended as a hypnotic, more reliable and better borne than chloral (Poppi). In the hands of others, on the contrary, its use was uncertain and accompanied by unpleasant secondary symptoms (Langgaard, Mairet, Schmitt).

APPENDIX.

The compounds included in this section will be found to fall into two main classes; viz., those which are, at least at present, of insufficient importance to require detailed description in the body of the work, and those which are not purely synthetical remedies.

All those of the former class are, however, met with and referred to in medical literature, and those of the latter are in many cases of established reputation, so that it has been thought desirable to embody some information respecting their properties and uses in an appendix. No attempt has been made for the present to deal with them in the form and with the completeness aimed at in the preceding pages; they are added rather for the convenience of the medical man and pharmacist than as an essential part of the book, and the information given is in most cases selected more with a view to practical usefulness than to exhaustive treatment. Should it be considered desirable this part of the work may be developed and extended in future editions, though it must be at once stated that there is great difficulty in coming at definite statements about many of the substances included.

ABRIN.

Nature and Source.—Active principle from the seeds of *Abrus precatorius*, Linné. A body of an albumenoid character believed to consist of two proteids, paraglobulin and α-phytalbumose, which closely resemble snake-venom in their action and properties, except that they undergo a complete change at a temperature below that of boiling water.

Properties and Uses.—A brownish-yellow powder, soluble in water. It is possessed of enormous poisoning potency, $\frac{1}{100}$ of a grain being a fatal dose for a man of 130 lbs. weight; the greatest care must, therefore, be taken in its use and storage. According to Prof. Kobert abrin produces the artificial conjunctivitis for which preparations of the seed are sometimes used in ophthalmology.

ADONIDIN.

Nature and Source.—A glucoside from the herb *Adonis vernalis*, Linné.

Properties and Uses.—A yellowish-white hygroscopic powder, readily soluble in water and alcohol; insoluble in ether, chloroform and benzene. When heated above 30° C. it is converted into a brownish-black mass.

In small doses adonidin increases the vigor of cardiac action, and is stimulant and feebly diuretic; is specially indicated in aortic and mitral insufficiency, relieving the praecardial pains, dyspnœa, palpitation, etc.

Dose.—The single dose of adonidin should not exceed 1 grain; it is preferably prescribed with carbonate of ammonium and chloroform water, in doses of $\frac{1}{6}$ to 1 grain four times a day.

Adonidin tannate is a brownish-yellow powder, taken up sparingly by water and not at all by ether, but readily soluble in alcohol.

ÆSCULIN.

$C_{15}H_{26}O_9$.

Nature and Source.—A glucoside from the bark of *Æsculus hippocastanum*, Linné.

Properties and Uses.—Lustrous white acicular crystals, soluble in hot water, forming a solution that in the dilution of 1 : 1,000,000 has a blue fluorescence (especially if acidified). For this reason it has also been termed "polychrome" and "bicolorin." Æsculin has been recommended as a substitute for quinine in remittent fever.

AGARICIN.

Synonym : Agaric or Agaricinic Acid.

$C_{14}H_{27}OH(CO_2H)_2H_2O$.

Nature and Source.—An active principle of the fungus *Polyporus officinalis*, Fries.

Properties and Uses.—A white, lustrous powder, consisting of microscopically small crystals, tabular in form. Cold water takes up very little agaricin, but when the solvent is boiling the substance is gradually dissolved with formation of froth; on cooling separation occurs. Agaricin melts at 138° C.

The principle is somewhat widely employed as a remedy against the exhaustive night sweats of consumptives, or to combat the sudorific action of the synthetical antipyretics. It appears to be well-borne and free from any marked secondary or after-effects.

Dose.—⅓ to ½ grain, in pills (⅙ gr. in each); best taken about 6 p. m.; if the action be insufficient, the dose may be increased to 5 pills.

ALANTOL.

$C_{20}H_{32}O$.

Nature and Source.—Liquid body from the root of *Inula helenium.*

Properties and Uses.—An aromatic liquid, boiling at 200° C. It has been recommended in tuberculous diseases as a substitute for oil of turpentine.

ALSTONINE.

Nature and Source.—An alkaloid from the bark of *Alstonia constricta*, Mueller, belonging to the Apocynaceæ.

Properties and Uses.—White, lustrous, silky crystals, which dissolve readily in ether, alcohol and chloroform; cold water does not take it up, but to hot water it communicates an intensely bitter taste.

Alstonine appears to possess antiperiodic, antiseptic and stimulant properties, combining the virtues of quinine and strychnine. Used in medicine against typhus fever.

It is also said to be used (or rather the bark) in the manufacture of pale ale, as a substitute for hops.

ANEMONIN.

$C_{15}H_{12}O_6$.

Nature and Source.—The active principle of the herb *Anemone pulsatilla*, Linné.

Properties and Uses.—Colorless crystalline needles, which melt at 152° C. and readily dissolve in warm alcohol, whilst they are insoluble in water and ether.

Although anemonin is not to be reckoned among the powerful poisons, it is a nerve poison which acts upon the central nervous system. It is recommended in whooping cough, bronchitis and asthma, as well as in dysmenorrhœa.

Dose.—The quantity daily given varies between 1 and 2 grains, administered in two portions as powder. Larger doses must be avoided.

ANISIC ACID.

$C_6H_4(OCH_3)COOH$.

Nature and Source.—An isomer of methyl-salicylic acid, obtained by the oxidation of anethol, a constituent of anise and fennel oils.

Properties and Uses.—Colorless prisms, belonging to the monoclinic system, which melt at 180° C. and sublime unchanged. Insoluble in cold water, but freely taken up by cold and hot alcohol.

The antiseptic and antipyretic properties of anisic acid have been employed on the one hand in the treatment of wounds, and on the other in acute rheumatism, etc. For internal use the crystalline and readily soluble sodium salt is recommended; it has an agreeable taste and reduces the temperature without weakening the heart's power, diminishing blood pressure, or disturbing the stomach.

Dose.—Of the sodium salt 15 grains; but the preparation is very little used.

APIOL.

$C_{12}H_{14}O_4$.

Nature and Source.—A camphor from the fruits of *Petroselinum sativum*, Hoffmann.

Properties and Uses.—White needles, of a feeble parsley odor, melting at 32° C. Apiol is insoluble in water, but alcohol or ether dissolve it freely.

This substance has been used in ague as an antiperiodic, and against dysmenorrhœa.

Dose.—For the former purpose 15 grains, but less for the latter.

Liquid apiol must not be confounded with this crystalline principle; it is merely an alcoholic extract of parsley seeds.

ARBUTIN.

$C_{12}H_{16}O_7, \frac{1}{2}Aq.$

Nature and Source.—A glucoside obtained from the leaves of bearberry, *Arctostaphylos uva-ursi.*

Properties and Uses.—Long, colorless, lustrous needles, which melt at 170° C. Cold water takes up one-eighth its weight of arbutin, while the same solvent at 100° C. dissolves an equal weight; one part is soluble in 16 parts of alcohol. Arbutin splits up when hydrolysed into hydroquinone (C_6H_4 $_2OH$. See p. 99) and sugar.

Affections of the urinary tract is the special branch of medicine in which arbutin is regarded as suitable, its action being ascribed to the hydroquinone set free in its decomposition in the organism.

Dose.—75 grains *pro die* in divided doses.

ARECOLINE.

$C_8N_{13}NO_2$.

Nature and Source.—An alkaloid, isolated primarily by E. Jahns, from the seeds of *Areca catechu*, Linné, which yield at most 0.1 per cent.

Properties and Uses.—A strongly alkaline liquid, soluble in every proportion in water, alcohol, ether or chloroform; b. p. 220° C.

Arecoline is the active anthelmintic principle of areca nuts, but is also a powerful poison, affecting the heart similarly to muscarine. Its use has been suggested in veterinary practice.

Dose.—$\frac{1}{15}$ to $\frac{1}{10}$ of a grain.

ASPIDOSPERMINE.

$C_{22}H_{30}N_2O_2$.

Nature and Source.—An alkaloid isolated from the bark of *Aspidosperma quebracho*, Schlechtendal.

Properties and Uses.—Colorless, prismatic crystals, insoluble in water, but taken up by 48 parts of alcohol or 106 parts of ether.

Aspidospermine is believed to stimulate the respiratory centres and assist the oxygenation of the blood. It is recommended in asthma, dyspnœa, emphysema, etc.

Dose.—¼ to ½ grain.

ATROPINE SALTS.

$C_{17}H_{23}NO_3\bar{A}$.

Nature and Source.—Various combinations of different acidulous radicals (represented in the above formula by $\bar{A}$), with the principal alkaloid from *Atropa belladonna, Datura stramonium.* The most important are described below:

Atropine oleate is prepared by dissolving 1 part of atropine in 30 parts of oleic acid and adding 50 parts of olive oil. Regarded as similar in action to extract of belladonna, and recommended as a substitute for it in the preparation of suppositories, since they can be made by it of more uniform composition.

Atropine santoninate, a substitute for the more readily decomposed sulphate. The effects last as long as the other. Concentrated solutions must be prepared warm.

BERBERINE.

$C_{20}H_{17}NO_4$.

Nature and Source.—An alkaloid obtained from various species of *Berberis* and other plants.

Properties and Uses.—A bright yellow powder, consisting of fine lustrous needles, with a strongly bitter taste.

In the form of *phosphate*, this principle has been recommended against malaria and the digestive disturbances with vomiting of pregnancy. Other salts are also prepared.

Dose.—Of the phosphate, 15 grains *pro die*.

BISMUTH SALTS.

A number of organic salts of bismuth have been introduced during the past few years, and some of them have attracted more or less attention. They will be found briefly described below:

Albuminate.—A bulky, white or pale grey powder, containing up to 9 per cent. of bismuth; it has been employed with success in America against gastric and intestinal cramps. The substance was given in daily quantities of 20 to 60 grains.

Benzoate, or *sub-benzoate*, is prepared by the interaction of an acid solution of nitrate of bismuth and an aqueous solution of sodium benzoate. A white, bulky powder, almost impalpable, used as a stimulant dusting powder in the treatment of torpid ulcers; has been specially recommended against soft chancres, a few days being sufficient to transform them into clean ulcers. The first application produces moderate burning.

Oxyiodide, or *sub-iodide*, may be obtained by a number of processes. It is a brick-red, specifically heavy powder, consisting of microscopically small, reddish, translucent, cubical crystals. Oxyiodide of bismuth is insoluble in any re-agent without decomposition. It was introduced to the notice of the medical world as an antiseptic similar in action to iodoform, but appears to have been abandoned.

Oleate was credited with emollient and mild astringent properties, and used in pustular skin affections and acne.

Salicylate, Bi $(C_7H_5O_3)_3Bi_2O_3$, contains about 76 per cent. of bismuth oxide and 23 per cent. of salicylic acid. It is an amorphous yellowish-white powder, entirely insoluble in water; neither alcohol, ether, nor chloroform should extract salicylic acid from it. Precautions have to be taken to avoid the use of carelessly prepared compounds or mixtures containing free salicylic acid, as they have an irritant action.

Externally, the basic salicylate of bismuth has been employed in medicine as an iodoform substitute in the treatment of wounds, ulcers, etc. Internally, it has made a reputation in chronic diseases of the digestive organs and intestines. It is reported to have proved useful in diarrhœas, and in preventing fermentation in the intestines after operation. In doses of 10 to 15 grains, two or three times a day, as powder, it does not seem to cause functional disturbances, even when given for a prolonged period.

Subgallate, $[(OH)_3C_6H_2CO_2Bi(OH)_2]$, an exceedingly fine, non-hygroscopic, perfectly odorless, saffron-yellow powder, unaffected by exposure to light and air; it is insoluble in ordinary solvents.

Under the fancy name "Dermatol," bismuth subgallate was introduced into medicine as a substitute for iodoform. The most valuable characteristics of the compound seem to be (1) its drying properties, by virtue of which it has also a more or less pronounced kolyseptic action, (2) its freedom from irritating properties, and (3) its great stability, which enables it to be sterilized by steam, if necessary. Although only recently introduced, a number of reports have appeared on its use, from which it appears that the subgallate of bismuth is an excellent vulnerary for wounds and burns, even of great severity, while it has also proved useful in the treatment of moist eczema, ulcers and diseases of the eye (Heinz and Liebrecht, Gläser, v. Rogner, Rosenthal, Sackur, Eversbusch, etc.). For the latter purpose its fine condition makes it very suitable. It has also given good results in diseases of the middle ear (Davidsohn, Doernberger), and in the treatment of dental caries (Tiburtius Hirschfeld). Bacteriologi-

cal experiment proves that it has active kolyseptic virtues. Bismuth subgallate may be applied as dusting powder (*per se*, or with starch, etc.), collodion or glycerine emulsion, ointment or gauze (10 to 20 per cent.)

Bismuth-cerium salicylate, a reddish-white powder, insoluble in water and alcohol. According to Salaya it is one of the most active preparations in the treatment of diseases of the gastric and intestinal mucous membrane. It is recommended particularly in diarrhœa and dysentery due to ulceration of the intestines.

BOLDIN.

Nature and Source.—Principle from the leaves of *Boldoa chiliensis*.

Properties and Uses.—This substance darkens rapidly on keeping. It is given as a tonic in liver diseases and in the treatment of biliary calculi; also in affections of the bladder, and as a hypnotic.

Dose.—3 grains daily, in capsules, or as a 5 per cent. enema.

BORIC ACID.

H_3BO_4.

A new combination of boric acid has been put forward quite recently as specially suitable for use in medicine.

Nature and Source.—When equal parts of borax, boric acid and water are heated together a solution is formed, from which, on cooling, the new compound separates in crystals.

Properties and Uses.—The substance forms hard, ringing crystals, soluble to the extent of 16 per cent. in cold water, though very slowly. Oversaturated solutions are best prepared with boiling water, and the liquid cooled by immersion in cold water until of blood temperature. According to Jaenicke there is no chemical substance possessed of equal kolyseptic powers to this, and at the same time non-irritating, non-poisonous, and stable. It is recommended in general surgery, and especially in diseases of the ear.

BRYONIN.

$C_{18}H_{30}O_{19}$.

Nature and Source.—A glucoside from the root of *Bryonia alba*, Linné.

Properties and Uses.—A colorless, amorphous body, with a bitter taste. Recommended as an antihæmorrhagic.

BURSIN.

Nature and Source.—A principle from the plant *Capsella bursa-pastoris*.

Properties and Uses.—A light-yellow, hygroscopic substance, with an astringent taste. Bursin appears to be possessed of styptic properties; it has been recommended for hypodermic injection as a substitute for ergot.

BUXINE.

Nature and Source.—An alkaloid from the bark of *Buxus sempervirens*; probably it is identical with beberine.

Properties and Uses.—A crystalline mass with a very bitter taste, insoluble in water, but taken up by alcohol.

Recommended as an antifebrile.

Dose.—15 to 30 grains.

CAESIUM SALTS.

Some of the salts and double salts of caesium,—a bivalent element belonging to the group of alkali metals,—especially the bromides, have been recommended as antepileptics of more pronounced activity than the alkaline bromides. They are, however, rare and expensive, and hence have not found ready adoption into materia medica.

CAFFEINE SALTS.

$C_8H_{10}N_4O_2\bar{A}$.

Among the very considerable number of new salts of caffeine which have been made and tentatively brought under notice during the past few years, the chief are: benzoate, hydrobromide, hydrochloride, lactate, nitrate, oxalate, phenylate, phtalate, salicylate, sulphate, tannate, triiodide and valerianate.

Besides these there is also a long list of double salts, such as the citrate of caffeine and ammonium (54 per cent. of alkaloid), the benzoate, bromide, cinnamylate, citrate and salicylate of caffeine and sodium (between 45.8 and 62.5 per cent. of alkaloid), the boro-citrate, citro-benzoate, citro-salicylate. Few, if any, have succeeded in attracting attention.

The *benzoate*, *salicylate* and *cinnamylate* of sodio-caffeine are regarded as especially suitable for use subcutaneously, owing to their ready solubility.

The *boro-citrate* combines the physiological action of caffeine with the antiseptic properties of boric acid; it is readily soluble.

The *carbolate* and *phtalate* have also been recommended for hypodermic injection, being readily soluble, and even in concentrated solution without irritating effect upon the mucous membrane.

CALCIUM SALICYATE.

$CaC_7H_4O_3,H_2O.$

Properties and Uses.—A white, crystalline powder, free from odor and taste; difficultly soluble in water. It has been recommended, either alone or in combination with bismuth salicylate, in the diarrhœa of children and in gastro-enteritis.

Dose.—8 to 24 grains.

CAMPHORIC ACID.

$C_8H_{14}(COOH)_2.$

Nature and Source.—A dibasic acid obtained by the action of nitric acid on camphor.

Properties and Uses.—White, acicular or scaly crystals, odorless, and with a feebly acid taste; m. p. 175° to 178°. Cold water takes up only little, but the same solvent hot dissolves it readily, as do alcohol and ether; also soluble in fatty oils.

Camphoric acid was first applied in 1888, in acute and chronic diseases of the respiratory tract, by Dr. Reichert, who used ½ to 6 per cent. solutions topically in angina, coryza, acute bronchitis, etc. Several authors have cured cystitis by injections of ½ to 2 per cent. solution, and recommended it against the night sweats of consumptives. More recently

Professor Schultzer and others have also recorded their conviction of the superiority of camphoric acid in such cases to other medicaments.

Dose.—Up to 30 grains.

CANNABINE.

Nature and Source.—An alkaloid isolated from the drug *Cannabis sativa*, Linné, or Indian hemp.

Properties and Uses.—A brown, syrupy liquid, recommended as a hypnotic.

Dose.—1 to 5 grains daily.

The *tannate* of cannabine is a yellowish-brown powder, insoluble in water or ether, slightly soluble in alcohol, freely so in water rendered slightly alkaline. In doses of 2 to 10 grains, with an average of 4 grains, it has been spoken of as a useful hypnotic, especially in nervous sleeplessness and acute mania, free from unpleasant secondary effects.

CANNABINONE.

Nature and Source.—A constituent of the flowering tops of *Cannabis sativa*, Linné.

Properties and Uses.—A balsamic, resinous body, insoluble in water, but taken up by alcohol, ether, chloroform and benzene, as well as by fatty and essential oils.

Cannabinone has a hypnotic action.

Dose.—½ to 1½ grains; the taste, which is far from agreeable, may be disguised by the addition of powdered coffee.

CANTHARIDIN.

$C_{10}H_{12}O_4$.

Nature and Source.—Active principle from the entire insects of *Cantharis vesicatoria* and other allied members of the Coleoptera.

Properties and Uses.—Colorless, four-sided tables, insoluble in water, difficultly soluble in cold alcohol, more readily in ether, in fatty oils, and most freely in chloroform; with caustic alkalies it forms salts soluble in water.

The principle has been used in place of cantharides in plasters, ointments, collodion, liquor epispasticus, etc. More

recently recommended in the form of a compound with alkalies (by Liebreich) in the treatment of tuberculosis by subcutaneous injection. The actual value of the method is still undetermined.

Dose.—1 cc. of a $\frac{1}{8}$ per mille solution.

CARDOL.

Nature and Source.—An active principle from the pericarps of *Anacardium occidentale.*

Properties and Uses.—An almost colorless oil, which gives a violet color with sulphuric acid, and with lime water a deep black color.

Medicinally cardol is used as a blistering agent.

CARPAINE.

$C_{14}H_{27}NO_2$.

Nature and Source.—An alkaloid extracted from the leaves of *Carica papaya,* Linné.

Properties and Uses.—Carpaine forms well-defined, beautiful crystals, with a very bitter taste; it melts at 115° C., and forms crystalline salts with acids.

The discoverer of the base (Greshoff) found by experiment that it was a cardiac poison; subsequent examination showed that subcutaneously it did not produce any irritation or abscess, while valuable results were produced in aortic insufficiency and stenosis, good effects being manifest within a few minutes of the injection. Recommended for the subcutaneous treatment of heart diseases.

Dose.—$\frac{1}{10}$ to $\frac{1}{6}$ grain subcutaneously every day, or every second day.

CARVACROL.

$C_{13}H_{14}O$.

Nature and Source.—A phenol existent in the essential oil of *Origanum species.*

Properties and Uses.—A thick oil that does not solidify at −25° C.; b. p. 233° to 235°.

Carvacrol possesses powerful antiseptic properties.

The *iodide* is a yellowish-brown powder, insoluble in water, but readily soluble in ether, chloroform and olive oil; it melts

at 90° C., and is unaffected by light. It has been employed like iodoform in substance, gauze, collodion ointment, etc., in the treatment of wounds and skin diseases.

CATHARTINIC ACID.

Nature and Source.—An active principle from the leaves of *Cassia species.*

Properties and Uses.—Brown, hygroscopic scales, readily soluble in water and in dilute alcohol.

Therapeutically this acid is a laxative.

Dose.—4 to 6 grains, or half as much for children.

CETRARIN.

$C_{18}H_{16}O_8$.

Nature and Source.—A bitter principle from the lichen *Cetraria islandica.*

Properties and Uses.—White, acicular crystals, with a bitter taste; readily soluble in boiling alcohol.

Intravenous injections of cetrarin increase the secretion of saliva, bile and pancreatic juice, and stimulate peristalsis. Since during its use the number of blood corpuscles increases, especially when they have been diminished below the normal by disease, the principle is considered indicated in chlorosis.

Dose.—Internally, 1½ to 3 grains; intravenously, ⅛ to ¼ grain per pound of body-weight.

CHROMIC ACID.

CrO_3.

Nature and Source.—The so-called chromic acid of commerce, obtained by the action of sulphuric acid upon potassium bichromate, is of course chromic anhydride or trioxide, CrO_3. The acid (the true formula of which is H_2CrO_4) is not known in the free state.

Properties and Uses.—Chromic anhydride occurs in long red rhombic needles or prisms, hygroscopic on exposure to air, and readily soluble in water. It is a powerful oxidizing agent, and in concentrated solution destroys organic matter.

Externally this compound has been used pure, or with an equal volume of water, as a caustic, in the treatment of condylomata, warty excrescences, hypertrophied tonsils, etc. Its employment is also recorded as a hæmostatic in dental surgery, in dilute solution (1 to 2½ per cent.) for painting on syphilitic ulcers of the tongue, and in 5 per cent. solution against perspiration and tenderness of the feet. In the latter case the feet are carefully washed and dried, and the solution painted on; care must be taken to avoid wounded places. Also used against ozæna and gonorrhœa in 1 per mille aqueous solution.

CHRYSAROBIN.

$C_{30}H_{26}O_7$

Nature and Source.—A principle obtained from a concretion found in the stem and branches of *Andira araroba.*

Properties and Uses.—A yellow crystalline powder, incompletely soluble in 200 parts of water, more freely in hot benzene, alcohol, chloroform, petroleum ether, strong acid and alkalies. It is used externally in the form of 10 per cent. preparations against psoriasis, herpes tonsurans, eczema, etc. It has also been recommended internally, as an emetic and aperient which acts promptly without prejudicially affecting the general well-being.

Dose.—For very young children 6 grains, for 12 years o age 9 grains, and for adults 15 grains. Generally 8 or 9 grains is a sufficient dose.

COCAINE SALTS.

$C_{17}H_{21}NO_4,\overline{A}.$

Among the number of new combinations of cocaine for which useful properties have been claimed are the benzoate, borate, citrate, hydrobromide, nitrate, oleate, phenylate, phtalate, saccharinate, salicylate, sulphate, tannate and tartrate.

Only three of these need be described.

The *borate* was recommended for eye-douches and subcutaneous injection, and said to be superior to all other cocaine salts on account of the permanence of the solution and the indifference of the acid.

The *nitrate* is specially suitable (Lavoux) in place of the hydrochloride for prescribing in combination with nitrate of silver in the treatment of diseases of the genito-urinary tract. Even large doses of the silver salt as injection do not cause pain when associated with an equal weight of cocaine nitrate.

The *phenylate* is a thick honey-like mass, soluble in 50 per cent. alcohol. It has been used subcutaneously as a local anæsthetic in dental surgery (Vian, Oefele); as a paint or liniment (1 per cent. in 30 per cent. alcohol) in all local pain; as an application in catarrhs of various mucous membranes (5 to 10 per cent. solution or powder with acetanilide).

CODEINE PHOSPHATE.

$C_{18}H_{21}NO_3, H_3PO_4, 1\frac{1}{2}Aq.$

This preparation is officially recognized in the latest edition of the Pharm. Germ.

Properties and Uses.—Fine white needles, with a bitter taste, readily soluble in water, difficultly so in alcohol; the aqueous solution has an acid reaction.

It is used in 10 per cent. solution in various mental diseases, and in the treatmant of morphinism.

Dose.—1½ to 2 grains daily.

COLCHICEIN.

$C_{21}H_{22}(OH)NO_5.$

Nature and Source.—A product of the hydrolysis of colchicine (*q. v.*).

Properties and Uses.—Slightly soluble in cold, readily so in boiling water, in alcohol and in chloroform.

Colchicein is very poisonous, acting chiefly on the cerebrum and spinal column. Used subcutaneously in the treatment of gout and acute rheumatism.

Dose.—$\frac{1}{60}$ to $\frac{1}{30}$ grain hypodermically.

COLCHICINE.

$C_{21}H_{22}(OCH_3)NO_5$.

Nature and Source.—A basic principle which occurs in all parts of the meadow saffron, *Colchicum autumnale*, Linné.

Properties and Uses.—An amorphous substance, which forms a crystalline double salt with gold, and a compound with chloroform of similarly definite form. In its hydrolysis colchicein and methyl alcohol are formed. It melts at 143° to 147° C., and is readily soluble in cold water, alcohol, and chloroform. Laevorotatory.

Like colchicein, the mother substance is a powerful poison; it has been recommended against gout, rheumatism, and sciatica.

Dose.—$\frac{1}{120}$ to $\frac{1}{60}$ grain.

CONESSINE.

$C_{20}H_{40}N_2$.

Nature and Source.—An alkaloid from the bark and Seeds of *Holarrhena africana* and *H. antidysenterica.*

Properties and Uses.—Delicate masses of acicular crystals, which melt at 121° C.; difficultly soluble in water, readily so in alcohol, ether, and chloroform.

Therapeutically conessine seems to possess useful properties for the treatment of dysentery and diarrhœa.

CONIINE HYDROBROMIDE.

$C_8\dot{H}_{17}N.HBr$.

Nature and Source.—Coniine occurs in the seeds chiefly of the hemlock, *Conium maculatum.*

Properties and Uses.—Hydrobromide of coniine occurs in crystalline form.

It reduces the frequency, duration, and intensity of the attacks of tetanus traumaticus; has also a paralysing effect upon the respiratory muscles. The salt has been recommended subcutaneously in the treatment of cardiac asthma.

Dose.—$\frac{1}{6}$ to $\frac{1}{2}$ grain for adults, $\frac{1}{12}$ to $\frac{1}{3}$ grain for children; subcutaneously $\frac{1}{6}$ to $\frac{1}{3}$ grain.

CONVALLAMARIN.

$C_{23}H_{44}O_{12}$.

Nature and Source.—A glucoside from the lily-of-the-valley. *Convallaria majalis*, Linné.

Properties and Uses.—A whitish-brown, amorphous powder, soluble in water and alcohol.

Therapeutically convallamarin has shown itself useful as a cardiac, resembling digitalin in action, but not cumulative.

Dose.—½ grain, gradually increasing to 5 grains.

CONVOLVULIN.

$C_{31}H_{50}O_{16}$.

Nature and Source.—The glucoside obtained from the root of *Ipomœa purga*; it is also yielded by some other plants of the same genus.

Properties and Uses.—A rubber-like, amorphous mass, with acid properties, irritant to the mucous membrane and sternutatory. Freely soluble in alcohol and acetic acid; practically insoluble in water, hot or cold.

Convolvulin is a powerful purgative.

Dose.—1½ to 3 grains.

CORNUTINE.

Nature and Source.—An alkaloid from the sclerotium of ergot, *Claviceps purpurea*, Tulasne.

Properties and Uses.—A very poisonous compound, the chemical nature of which is still uncertain; its salts are stable.

It exerts a contractile effect upon the vascular system, and is recommended in hæmorrhage from abortion, and to increase the vigor of the pains in labor. According to Prof. Kobert, cornutine is the true active principle of ergot.

Dose.—$\frac{1}{12}$ to $\frac{1}{6}$ grain.

COTOIN.

$C_{22}H_{16}O_6$.

Nature and Source.—A neutral principle from the bark of species of *Nectandra*.

Properties and Uses.—A pale yellow, amorphous or crystalline powder, slightly soluble in water, freely so in ether, chloroform, alcohol and alkalies.

Cotoin is said to check salivation and night-sweats, and to have a specific action on the intestinal tract in cholera.

Dose.—½ to 2 grains dissolved in acetic ether (1:4).

CREATINE.

$C_4H_9N_3O_2$.

Nature and Source.—A natural constituent of various tissues of the animal body, especially of muscle.

Properties and Uses.—An opaque white solid, odorless, but with a bitter and acrid taste. The monohydrate occurs in transparent prisms, soluble in 70 parts of water.

Medicinally creatine has been recommended as a remedy for atony of the muscular system or digestive organs.

Dose.—1½ grains several times a day.

CUBEBIC ACID.

$C_{28}H_{30}O_7$.

Nature and Source.—A principle obtained from the fruits of *Piper cubeba*, Linn. fil.

Properties and Uses.—A white, wax-like substance, which turns brown on exposure to the air; readily soluble in alcohol and ether.

Cubebic acid is believed to be the source of the antiblennorrhagic property of cubebs.

Dose.—Up to 15 grains.

CURARINE.

$C_{18}H_{35}N$. (?)

Nature and Source.—An alkaloidal principle, which occurs as sulphate in "curare," the arrow poison of the Indians, prepared from an extract of various species of *Strychnos*.

Properties and Uses.—An amorphous substance, which gives a red color with concentrated sulphuric acid. Also in colorless, hygroscopic prisms, with a very bitter taste, readily soluble in water and alcohol, difficultly so in chloroform.

This principle is a powerful poison, which produces a general paralysing effect.

CYTISINE.

$C_{11}H_{14}N_2O$.

Nature and Source.—An alkaloid obtained from *Cytisus laburnum* and other species.

According to recent investigations, the same body is met with in *Ulex europæus*, though there it has been termed ulexine.

Properties and Uses.—In yellowish-white, deliquescent crystals; chiefly used in the form of *nitrate*, a beautiful crystalline salt, pale yellow in color, and acid in reaction.

Therapeutically cytisine stands between strychnine and curare, and has been used as nitrate subcutaneously in paralytic migraine; also diuretic in dropsy and cardiac diseases.

Dose.—$\frac{1}{20}$ to $\frac{1}{12}$ grain hypodermically.

DATURINE.

$C_{17}H_{23}NO_3$.

Nature and Source.—An alkaloid from the leaves and seeds of *Datura stramonium*, Linné, regarded as identical with hyoscyamine.

Properties and Uses.—Physically daturine exactly resembles hyoscyamine, and the analogy holds good of the physiological action upon the pupil.

The sulphate, which is generally employed, occurs in minute white granular crystals. Given to a patient suffering from acute mania it was successful in producing sleep.

DELPHININE.

Nature and Source.—An alkaloid from the seed of *Delphinium staphisagria*, Linné.

Properties and Uses.—From ethereal solutions the compound crystallises in small rhombs, scarcely taken up by water, but freely so by alcohol and chloroform; taste bitter.

Physiologically it has a powerful action on the heart like aconitine.

Dose.—Internally $\frac{1}{3}$ to 1 grain *pro die*.

DIGITALEIN.

Nature and Source.—A glucosidal principle from the leaves of *Digitalis purpurea*, distinguished from a number of other similar preparations by the suffix "Schmiedeberg."

Properties and Uses.—A pale yellow amorphous powder, readily soluble in water and absolute alcohol; the aqueous solution froths abundantly. It is said to combine the properties of digitalin and of digitoxin (*q. v.*)

DIGITOXIN.

$C_{21}H_3O_7$. (?)

Nature and Source.—The most poisonous of the four or five glucosides which make up commercial "digitalin," extracted from the leaves of *Digitalis purpurea*, Linné.

Properties and Uses.—Digitoxin is insoluble in water, and when subjected to hydrolysis does not yield sugar, but products (toxiresin, digitaliresin) which have no cardiac action, but excite clonic and tonic spasms. It occurs in white tufts of acicular crystals, with a very bitter taste; perfectly soluble in chloroform.

Dose.—$\frac{1}{200}$ to $\frac{1}{100}$ grain twice daily.

DUBOISINE.

$C_{17}H_{23}NO_3$.

Nature and Source.—An alkaloid obtained from the leaves of *Duboisia myoporoides*, R. Brown; believed to be chemically identical with or an isomer of hyoscyamine.

Properties and Uses.—Physiologically duboisine is much stronger than hyoscyamine, and acts as a mydriatic more rapidly than atropine and with less irritation; hence it is regarded as better suited for inflammatory affections. Requires to be used with caution.

The *sulphate* is similar in its medicinal properties to the alkaloid; is used in solution (1 grn. to the ounce) for the eye.

Dose.—$\frac{1}{120}$ to $\frac{1}{60}$ grain internally or subcutaneously.

EPHEDRINE.

Nature and Source.—An alkaloid from the leaves of *Ephedra vulgaris.*

Properties and Uses.—Colorless, stable crystals. The *hydrochlorate,* in which form the base is principally used, occurs as colorless needles, readily soluble in water.

Ephedrine has been recommended as a mydriatic in the place of homatropine. A 10 per cent. aqueous solution of the hydrochloride is used for instillation into the eye, for the purposes of investigation, and a 1 per cent. aqueous solution for daily use, 2 to 3 drops being instilled into the eye several times a day.

ERGOTININE.

$C_{35}H_{40}N_4O_6$.

Nature and Source.—A weak base, obtained from the sclerotium of ergot, *Claviceps purpurea,* Tulasne.

Properties and Uses.—Occurs in colorless, prismatic needles, soluble in alcohol; on exposure to light and air they rapidly darken, absorbing oxygen. In dilute solutions ergotinine is fluorescent, with a violet color.

According to the researches of Kobert this principle, if quite pure (free from cornutin and sclerotinic acid), is inert.

ERYTHROPHLŒINE.

Nature and Source.—An alkaloid from an ordeal bark yielded by the *Erythrophlœum guineense,* a tree of the Leguminous order, found in West Africa.

Properties and Uses.—The hydrochloride of erythrophlœine forms whitish crystals, soluble in water.

This alkaloid is a cardiac, said to be more powerful than ordinary "digitalin." Some years ago claims were made for it as a local anæsthetic; further investigation led to the result that the statements appear to be unfounded.

ESERIDINE.

$C_{15}H_{23}N_3O_3$.

Nature and Source.—An alkaloid from calabar beans,

the seeds of *Physostigma venenosum*, Balfour, where it occurs in conjunction with eserine (physostigmine).

Properties and Uses.—Eseridine melts at 132° C. (eserine 90° C.), and is difficultly soluble in ether.

Physiologically eseridine resembles eserine, but is six times weaker in action. It has been recommended as a purgative for herbivorous animals in veterinary practice, but seems to have a tendency to act as a cardiac poison; further, if not perfectly dissolved, it may cause gangrene when subcutaneously injected.

EUCALYPTOL.

$C_{10}H_{18}O$.

Nature and Source.—An oxygenated body, first isolated by E. Jahns from the essential oil of various *Eucalyptus* species. Has also been detected in the oils of a considerable number of other plants.

Properties and Uses.—Pure eucalyptol is a colorless liquid, with a camphoraceous odor; sp. gr. 0.930, b. p. 176° to 177° C., and crystallizing point −1° C. It is practically insoluble in water, but miscible with alcohol, ether, chloroform and fatty oils. Optically the compound is inactive.

Externally eucalyptol has been used as a stimulant in rheumatism and neuralgias, and, further, in the antiseptic treatment of atonic ulcers, gangrene, etc. Internally it plays an important part in diseases of the lungs and of the respiratory system generally. The recent literature of the medicinal use of eucalyptol records its more or less successful administration in tuberculosis, pulmonary gangrene, pneumonia, irritable cough, incipient phthisis, etc. It was also very largely used during the late influenza epidemics for saturating the atmosphere with antiseptic vapor, in order to keep off attacks. There is some evidence that eucalyptol is of value in the treatment of malaria, either internally or subcutaneously, mixed with oil.

Dose.—5 drops in gelatine capsules, or in emulsion, for internal administration; the same dose may be given hypodermically, mixed with oil.

EUGENOL.

$C_6H_3.C_3H_5(OH)(OCH_3)$.

Nature and Source.—A phenol, found in many essential oils, especially those of cloves, pimento, cinnamon, sassafras, bay.

Properties and Uses.—An aromatic, oily liquid, boiling at 235° C. On exposure to the air it turns brown. Readily soluble in alcohol, but only very sparingly so in water; it forms compounds of definite character with caustic alkalies.

Eugenol is a powerful antiseptic, regarded as superior in this respect to phenol. Having an agreeable odor it is well suited for use in dental surgery. Has also been recommended as a febrifuge, but not much employed.

Dose.—45 minims *pro die*, dissolved in spirit and diluted with water.

Two derivatives of eugenol have recently been brought under the notice of the medical world, which may be briefly mentioned here:

Benzoyl-eugenol, $C_6H_3.C_3H_5(OCH_3)CO_2C_6H_5$, occurs in neutral acicular crystals, which melt at 70.5° C., are free from color and odor, and have a feebly bitter taste. Scarcely taken up by water, but freely by hot alcohol, by chloroform, ether and acetone.

Cinnamyl-eugenol, $C_6H_3.C_3H_5(OCH_3)CO_2(CH)_2C_6H_5$, forms neutral, lustrous needles, free from color, odor and taste; m. p. 90° to 91° C. Scarcely soluble in water, but readily in the other solvents named above.

These compounds are being clinically tried in the treatment of tuberculous affections.

EUONYMIN.

Nature and Source.—A resin from the root and stem-bark of *Euonymus atropurpureus*, Jacquin.

Properties and Uses.—A brown or greenish-brown hygroscopic powder, with a feebly bitter taste, soluble in water, almost insoluble in alcohol and ether.

Medicinally the dry extracts of euonymus bark, known as euonymin, are used as hepatic stimulants, being especially

recommended in constipation due to hepatic torpor. Though laxative, euonymin is not nearly so active an irritant of the intestines as podophyllin.

Dose.—½ to 3 grains.

FILICIC ACID.

(AND ANHYDRIDE.)

$C_{14}H_{16}O_5$.

Nature and Source.—A principle from the rhizome of *Aspidium filix-mas*, Swartz.

Properties and Uses.—Filicic acid is a yellowish powder, consisting of microscopic, rhombic scales.

According to the most recent pharmacological investigations the crystalline filicic acid is absolutely inert (Poulson). The anthelmintic properties of male-fern extract must be ascribed to an amorphous filicic anhydride, which if absorbed into the system is distinctly toxic. As its absorption is favored by the presence of fatty oils, in which it is soluble, it is recommended not to prescribe castor oil after the extract but to select some other purgutive.

GELSEMINE.

$C_{54}H_{69}N_4O_{12}$.

Nature and Source.—An alkaloid which occurs in the rhizome of *Gelsemium nitidum*, Michaux, associated with gelseminine (*q. v.*).

Properties and Uses.—A brittle, transparent, solid mass, crystallizing with difficulty from alcohol. It fuses at 45° C. to a colorless acid liquid, which on cooling solidifies to a transparent vitreous mass; at higher temperatures it is entirely dissipated. Cold water scarcely takes it up at all, and from the same solvent hot it separates on cooling in a granular amorphous form. It forms salts which, except the sulphate, are crystalline.

Gelsemine is regarded as the active principle of gelsemium and, hence, is credited with valuable properties in the treatment of neuralgia, toothache, convulsive cough, etc. It is said to be an antidote to strychnine.

Dose.—$\frac{1}{60}$ to $\frac{1}{20}$ grain.

GELSEMININE.

Nature and Source.—An alkaloid tha. .s extracted together with gelsemine from the rhizome of the yellow jasmine, *Gelsemium nitidum*, Michaux.

Properties and Uses.—A dark-brown, resinous mass, permanent in the air. When powdered it has a yellow color, and a bitter taste resembling that of the rhizome. Water takes up very little, but alcohol, ether and chloroform dissolve it readily. It is a strong base, forming neutral amorphous salts with acids.

The medicinal properties of gelseminine do not seem to have been made out, or indeed its nature chemically.

GOLD SALTS.

Quite a number of gold compounds, salts and double salts, as well as the precipitated metals, have been introduced into medicine, such as :

Sodium auro-chloride. A golden yellow powder, which feebly attracts moisture. It contains at least 30 per cent. of gold. Readily soluble in water, but only partly so in alcohol. Organic substance and most salts (as also light) decompose the solutions.

Like all gold preparations this double salt has been used in syphilis, either in the form of simple solutions or as lozenges with chocolate.

Dose.—$\frac{1}{6}$ to 1 grain several times a day.

Gold chloride. Occurs in long orange crystals, very hygroscopic, readily soluble in water, alcohol and ether.

Internally this corrosive compound produces general symptoms allied to those of mercuric chloride. Externally it has been applied as powder by rubbing into the tongue ($\frac{1}{6}$ to $\frac{1}{4}$ grain), and as concentrated solution for the cauterizing of cancer.

Gold monobromide. This forms a yellowish-grey, very friable mass, insoluble in water. It has been employed in Russia, Germany and Belgium as a nervine and antiepileptic. According to some observers it is better borne than any of the bromides.

Dose.—For children $\frac{1}{20}$ to $\frac{1}{10}$ grain; adult dose $\frac{1}{8}$ grain, increasing to $\frac{1}{5}$. Against migraine $\frac{1}{20}$ grain, twice daily, one hour before meals.

Other compounds of the metal, such as cyanide, iodide, oxide, etc., have also been tried in the treatment of syphilis, but not generally. A so-called "bichloride" was represented to be the remedy employed in the Keeley cure for drunkenness.

GUARANINE.

v. CAFFEINE.

GYNOCARDIC ACID.

$C_{14}H_{24}O_2$. (?)

Nature and Source.—The active principle from the oil of the seeds of *Gynocardia odorata*, R. Brown.

Properties and Uses.—A yellowish, unctuous solid, melting at about 30° C.; it has a burning and acrid taste, and a marked odor.

Gynocardic acid is used internally and externally, like chaulmoogra oil, in the treatment of leprosy and syphilis, and of gouty and rheumatic affections. It is regarded as superior to the oil.

Dose.—½ to 3 grains; externally as liniment with oil (1: 10 to 20).

HAEMOGLOBIN.

Nature and Source.—The red coloring principle of the blood.

Properties and Uses.—A doubly refractive, pleochromatic colloid or crystalline substance.

Given, owing to its content of iron, in an organic and presumably easily assimilated form, in anæmia and chlorosis.

Dose.—1½ to 3 drachms daily, in wine, tablets with chocolate, etc.

It may be interesting to add that the haemoglobin of the dog has been represented by the following extraordinary formula: $C_{636}H_{1025}N_{164}FeS_3O_{181}$.

HELENIN.

C_6H_8O.

Nature and Source.—A stearoptene from the root of *Inula helenium*, Linné.

Properties and Uses.—Colorless, crystalline, neutral needles, melting at 110° C. Practically insoluble in water, but freely taken up by hot alcohol, by ether and by oils. It passes over undecomposed with the vapors of water.

Helenin has been used medicinally as a demulcent and antiseptic in whooping cough, chronic bronchitis, the diarrhœa of consumptives, etc.

Dose.—1/6 of a grain, or 6 grains *pro die*.

HELLEBOREIN.

$C_{26}H_{44}O_{15}$.

Nature and Source.—A glucoside from the rhizome of species of *Helleborus*, where it occurs in association with helleborein.

Properties and Uses.—A crystalline compound freely soluble in water.

Helleborein has been used as a substitute for digitalis, either internally (as pills or with some viscid vehicle) or hypodermically—a mode of employment for which its ready solubility specially makes it suitable. In certain ophthalmological operations its anæsthetic action has been called into requisition, and for this purpose it is said to be superior to cocaine.

HOMATROPINE.

$C_{16}H_{21}NO_3$.

Nature and Source.—First synthetically obtained by Ladenburg from tropic acid and tropin, two derivatives of atropine. On the large scale it is a bye-product in the preparation of atropine.

Properties and Uses.—White, crystalline, readily soluble, clear prisms.

The physiological action of homatropine closely resembles that of atropine; it dilates the pupil very rapidly and

energetically, but the effect passes off sooner than that of atropine. Also given against the night-sweats of phthisis. The salts chiefly employed are the *hydrobromide* (official in the B. P.), *hydrochloride*, *salicylate*, and *sulphate*.

Dose.—Homatropine is prescribed in the same doses and forms as atropine.

HYDRASTINE.

$C_{21}H_{21}NO_6$.

Nature and Source.—An alkaloid from the rhizome of *Hydrastis canadensis*, Linné.

Properties and Uses.—White, four-sided, rhombic, lustrous prisms. Also occurs in an amorphous form, and in various salts. Hydrastine is almost insoluble in water, but is taken up by ether, alcohol, and chloroform.

The alkaloid has been credited with the property of increasing the energy, number, and duration of uterine movements, and therefore recommended in metrorrhagia. Also internally in typhoid conditions, in dyspepsia, as an intermittent, and externally in hæmorrhoids, aphthæ, skin diseases.

The *nitrate*, which occurs in yellow crystals, m. p. 120° C., and the *tartrate* of hydrastine, a yellowish-white, crystalline powder, soluble in hot alcohol and water, are also prepared.

HYDRASTININE.

$C_{11}H_{13}NO_3$.

Nature and Source.—An oxidation product of hydrastine described above.

Properties and Uses.—Acicular crystals, melting at 116° to 117° C., readily soluble in alcohol, ether, and chloroform. It forms soluble salts with most acids; the hydrochloride is most suitable for medicinal purposes.

Two or three subcutaneous injections have been found very effective against uterine hæmorrhage, dysmenorrhœa, etc.

Dose.—1 grain in 10 per cent. solution; the injections are best made in menstrual irregularities previous to the expected term.

HYOSCINE.

$C_{17}H_{23}NO_3$.

Nature and Source.—Occurs in the seeds of *Hyoscyamus niger*, Linné, associated with hyoscyamine.

Properties and Uses.—Hyoscine is itself non-crystalline; it is split up on hydrolysis into tropic acid and pseudatropine. The gold double salt melts at 196° to 198° C.

In the form of halogen salts, of which the hydrobromide is the chief, hyoscine is used as a sedative and hypnotic in various mental diseases, in asthma and neuralgias.

Hyoscine hydrobromide forms fine colorless, rhombic crystals, soluble in water and alcohol, forming feebly acid solutions, with a bitter somewhat pungent taste.

Dose.—Internally $\frac{1}{100}$ to $\frac{1}{30}$ grain, two or three times daily, in pills or solution; subcutaneously $\frac{1}{250}$ to $\frac{1}{50}$ grain. As a mydriatic a 1 per cent. solution is employed.

INULIN.

$(C_6H_{10}O_5)_2$.

Nature and Source.—A principle from the root of *Inula helenium*, of dahlias, sun-flower, dandelion.

Properties and Uses.—A white powder, which consists of double refracting crystals, readily soluble in water and in double salts of copper and ammonia. Laevorotatory. Inulin is not fermentable by yeast, and is scarcely affected by diastase or ptyalin.

By virtue of its resistance to the action of ferments inulin has been recommended for the preparation of inulin bread for diabetics. Is also said to have proved useful as a stimulant expectorant.

Dose.—1 to 3 grains.

IODINE CYANIDE.

CNI.

Properties and Uses.—Colorless needles, with a pungent odor; difficultly soluble in water, more readily in alcohol and ether; melting point 146.5° C.

This compound of iodine and cyanogen appears to be a powerful poison to the blood and protoplasm; it is, however, much less toxic than the pure hydrocyanic acid. According to Kobert the preparation is universally destructive to the lower forms of life, and may therefore prove very useful for preserving entomological collections, taxidermic preparations, furs, and the like from the attacks of insects, etc.

IRON COMPOUNDS.

Properties and Uses.—The most important of the newer compounds of iron are those classed as "indifferent," such as the *albuminates*, *peptonates*, etc. According to many authors these combinations of iron, which may be regarded as probably approximating to the natural forms in which the metal is present in the animal system, possess a very marked value in anæmia and chlorosis, where the prolonged administration of iron is indicated.

The indifferent preparations of iron are free from the astringency and chemical activity of iron salts as a rule, and hence have not injurious action on the teeth, nor any tendency to cause digestive disturbances. It is claimed for them that they are readily absorbed and highly active forms for the administration of iron.

KOUSSEIN.

Nature and Source.—A principle isolated from the flowers and unripe fruits of *Hagenia abyssinica*, Willd.

Properties and Uses.—A resinoid, amorphous, yellowish crystalline powder, with a bitter, pungent taste; readily soluble in alcohol, ether, and alkalies; very little so in water.

Koussein is recommended as a substitute for cusso (kousso) as an anthelmintic.

Dose.—15 to 30 grains, divided into four doses, to be taken at intervals of half an hour. The last quantity is followed by a dose of castor oil.

LACTUCINE.

Nature and Source.—The active principle of the concrete juice (lactucarium) of *Lactuca virosa*, Linné.

Properties and Uses.—White scales, soluble in 60 to 80 parts of cold water, or in alcohol.

Lactucine has the reputation of being a sedative and hypnotic.

Dose.—1 to 5 grains.

It is worthy of note that hyoscyamine has been found (Dymond) in the extracts of various species of *Lactuca*; the properties of lactucarium may be due to the presence of this alkaloid.

LAMINE.

Nature and Source.—An alkaloid from the flowers of the dead-nettle, or white archangel, *Lamium album*.

Properties and Uses.—Lamine is credited with powerful haemostatic properties, and in the form of *sulphate* has been recommended for hypodermic injection.

LANTANINE.

Nature and Source.—An alkaloid from the herb *Lantana brasiliensis*.

Properties and Uses.—Antiperiodic and antipyretic properties have been ascribed to lantanine, and cases are recorded in which its use proved successful where quinine had failed.

Dose.—15 to 30 grains daily.

LEPTANDRIN.

Nature and Source.—A glucoside, obtained from the rhizome of *Veronica* (*Leptandra*) *virginica*, Linné.

Properties and Uses.—Leptandrin stimulates the biliary secretion and is purgative.

Dose.—1 to 3 grains as a hepatic stimulant; 8 grains produce purging without diarrhœa.

LITHIUM SALICYLATE.

$LiC_7H_5O_3, \frac{1}{2}Aq.$

Properties and Uses.—A white, crystalline powder, soluble in little more than its own weight of water; also abundantly taken up by alcohol.

According to Vulpian this salt will usefully supplement the action of sodium salicylate, as it removes the last traces of fever in acute articular rheumatism, which often obstinately resist the administration of the sodium combination. Against chronic rheumatism and rheumatic affections of the tendons it is superior to the latter.

Dose.—1 drachm daily.

LOBELINE.

Nature and Source.—An alkaloid from the herb and seeds of *Lobelia inflata*, Linné.

Properties and Uses.—A yellowish, syrupy liquid, darkening on keeping.

Medicinally, lobeline is used as *sulphate*, which, prepared from the leaves, is a yellowish-white powder, less hygroscopic than the yellowish, granular mass which is obtained from the seeds. It has been recommended in the treatment of bronchitic dyspnœa and spasmodic forms of asthma.

Dose.—1 to 6 grains, internally or subcutaneously.

MAGNESIUM SALICYLATE.

$[C_6H_4(OH)CO_2]_2Mg, 4Aq.$

Nature and Source.—This salt is prepared by the interaction, at high temperatures, of salicylic acid and magnesium carbonate.

Properties and Uses.—Long, colorless, hygroscopic crystals, readily soluble in water and alcohol, and with a bitter taste.

Magnesium salicylate was recommended by Huchard in abdominal typhus, as a valuable agent for freeing the intestinal canal from infectious substances. Even in cases where there was much diarrhœa its use is not held to be contraindicated,

as slight, laxative effects only are produced when large doses are given.

Dose.—45 grains to 1½ drachms daily, as powder, or in aqueous solution.

MANGANESE COMPOUNDS.

When manganese was found to be a natural constituent of the blood, its use was naturally suggested in anæmia and similar impoverished conditions of that fluid. Owing, however, to the insolubility of many of its compounds, and the questionable value of those primarily selected, the employment of the metal in medicine gradually fell out of use; even such soluble forms as the *chloride* and *sulphate* proved to be exceedingly liable to change. Recently, certain so-called "indifferent" preparations of manganese have been prepared and recommended for use in medicine, which may be briefly described:

Albuminate occurs as yellowish-white scales, forming, with water, a clear solution.

Saccharate is a brown powder, containing 3 per cent. of manganese; similarly soluble in water.

Other similar preparations are the "dextrinate," "mannitate" and "peptonate," but the two above described have, so far, chiefly attracted attention in the treatment of chlorotic conditions, either alone or in various combinations with the analogous indifferent preparations of iron.

MECONARCEINE.

Nature and Source.—Variously described as a derivative of narceine ($C_{23}H_{29}NO_9$), one of the rarer bases of opium, and as an arbitrary mixture of various opium constituents.

Properties and Uses.—Lemon-yellow crystals, fairly soluble in boiling water, less so in strong alcohol, but somewhat more freely in 50 per cent. alcohol. The preparation has an acid reaction, and melts, with some decomposition, at 126° C.

Meconarceine is said to have proved very effective, internally administered, in neuralgia, insomnia, morphinism and bronchitic affections.

MENTHOL.

$C_{10}H_{19}OH$.

Nature and Source.—A stearoptene, obtained from the essential oils of various species of *Mentha* growing in Japan and North America.

Properties and Uses.—Colorless, prismatic, or circular crystals, with a peculiar, peppermint-like odor; m. p. 42° C.; b. p. 212° C. Slightly soluble in water, readily in oils, in ether and in alcohol.

Menthol is anæsthetic and disinfectant. Internally it has been used as a stomachic and carminative against cardialgia, colic, the vomiting of pregnancy, as also against phthisis. Externally it has made a reputation in the treatment of neuralgias and migraine, in the form of snuff against catarrh, ozæna. Inhalations have been adopted in influenza and pulmonary tuberculosis.

Dose.—1½ to 3 grains several times a day, in pills or spirituous solution.

Menthol benzoate is prepared by adding benzoic acid to the menthol designed for pencils; the counter-irritant effect upon the skin is increased.

Chloral-menthol is a stable, oily liquid, obtained by heating a mixture of equal parts of chloral and menthol on a water-bath, to at most 36° C. It has done good service in facial neuralgia, migraine, toothache, etc.

MERCURY COMPOUNDS.

It would be well to point out that the literature of all these compounds is very meagre; the greater number were introduced for hypodermic injection as anti-syphilitics, but no one of them seems to have as yet displaced at all generally the emulsions of calomel, yellow oxide, and mercurial ointment.

Mercuric and zinc cyanide.—This preparation, a white powder, entirely insoluble in water, was recommended by Sir J. Lister as an antiseptic, non-irritating dressing. It consisted of a certain proportion of mercuric cyanide (not exceeding 36 per cent.), the particles of which were "occluded" from the action of water by the insoluble zinc cyanide (Dunstan). In a later paper the chemist named details experiments held to

prove that the preparation is a chemical compound with the formula $Zn_4Hg(CN)_{10}$. It does not seem to have given in other hands such satisfactory results as were recorded by the eminent surgeon named.

Mercuric benzoate $(C_6H_5COO)_2Hg, H_2O$.—Small crystals, free from color, taste, and odor, sparingly soluble in cold, more readily in hot water, and in alcohol. In solution in brine, or suspended in liquid paraffin, was used by Stukowenkow subcutaneously against syphilis, and also by Cochery, one syringeful daily being given of a solution of the benzoate, sodium chloride and water, in the respective proportions 3:1:400. If cocaine were added, in order to relieve the slight pain of the injections, it would produce a separation of mercury.

Mercuric carbolate or *phenylate* $(C_6H_5O)_2Hg$.—Occurs as colorless needles, practically insoluble in water and cold alcohol, but taken up by hot alcohol (1:20), by ether, or a mixture of alcohol and ether, and by glacial acetic acid. Used against syphilis by Schadeck, in doses of $\frac{1}{3}$ to $\frac{1}{2}$ grain (children $\frac{1}{15}$ to $\frac{1}{12}$ grain) twice or three times a day.

Mercuric formamidate is a solution obtained by the action of formamide upon mercuric oxide. It does not coagulate albumen, is rapidly absorbed, and excreted with the urine.

Mercuric imido-succinate $[C_2H_4(CO)_2N]_2Hg$.—First described in 1852 by Dessaignes, and recommended by v. Mering and Vollert in 1888 as an antisyphilitic. It forms a white, lustrous, crystalline powder, which gives a clear solution with 25 parts of water, or 300 parts of alcohol. Subcutaneously injected in doses of $\frac{1}{5}$ grain. An addition of cocaine can be made without decomposing the salt.

Mercuric naphtolate.—A lemon-yellow powder, odorless, insoluble in water; contains 30.8 per cent. of mercury. The dose for internal administration is 1 grain. Naphtolacetate of mercury (similar in constitution to thymolacetate, *q. v.*) is a white, crystalline substance. These compounds were tried by Jaddasohn and Zeissing, but found to produce more violent pain than the thymolacetate or salicylate of mercury.

Mercuric oxycyanide.—$Hg_2O(CN)_2$ has been spoken highly of as an antiseptic by Boer, according to whom it is superior to sublimate as a germicide, while it is neutral, does not coag-

ulate albumen, is less caustic, and does not attack instruments so powerfully.

Mercuric peptonate.—A yellowish liquid, with a saline, feebly metallic taste, and slight acid reaction. Was introduced as a mild and efficient mercurial for hypodermic injection, not causing pain, nor producing abscesses. The usual dose was given as 1 ccm., said to correspond to 1/6 grain of mercuric chloride. A modification of this preparation has been quite recently brought under medical notice; viz.,

Glutine-peptone sublimate, described as a double compound of glutine peptone hydrochloride (made by the action of hydrochloric acid on gelatine) with sublimate, containing 25 per cent. of the latter. It forms a white, lustrous powder, hygroscopic, but very stable; is almost solely offered in the form of a 1 per cent. solution. The dose used by Dr. Hüfler was a Pravaz syringeful of solution, which corresponded to about 1/6 grain of mercuric chloride. The injections were described as accompanied by little pain and no severe local symptoms, while rapid and efficient in action on the disease.

Mercuric salicylate $C_6H_4OCO_2Hg$.—A fine, white, neutral powder, free from odor or taste, forming soluble double salts with the halogen chlorides, bromides, or iodides. It was first recommended in 1887 by Silva-Aranjo, and later by Schadek, as a mild but energetic mercurial for internal and external use. Internally the dose was 1/60 to 1/8 grain, chiefly in pill form; externally it was prescribed in 0.4 per mille solution as an injection in gonorrhœa, and suspended in mucilage for intra-muscular injection. Has perhaps been more widely used than any other of the newer compounds of mercury, having the advantage of convenience in use, absence of poisoning symptoms, and promptness of action; it seems, however, to be inferior in reliability of effect to some other mercurials.

Mercury sozoiodol (*v.* **Sozoiodol**).

Mercury tannate.—Somewhat dull brownish-green scales, free from odor and taste; yields tannin to water or alcohol, but is not *per se* soluble in these liquids. Was recommended as an anti-syphilitic by Lustgarten, its beneficial action being

ascribed to its decomposition by the alkaline fluids of the intestine, metallic mercury being set free. Dose 1 to 2 grains, half to one hour after food.

Mercuric thymolate $(C_{10}H_{13}O)Hg\text{-}HgNO_3$.—When pure, this compound, first recommended in England, is said to be perfectly colorless and free from odor, though on exposure it gradually becomes reddish, and acquires a faint thymoloid odor. The so-called *thymolacetate* of mercury has the formula $(C_{10}H_{13}O)Hg\text{-}HgC_2H_3O_2$. Both these compounds (as also a "thymolsulphate") were examined by Kobert, and shown to be suitable for therapeutical use against syphilis; chiefly the thymolacetate was employed, in doses of $\frac{1}{12}$ to $\frac{1}{6}$ grain, internally, as pill, or for intra-muscular injection, suspended in paraffin. Pain and infiltration were rare. The administration of thymolacetate of mercury by intra-muscular injection, with the simultaneous internal administration of potassium iodide, has also been warmly recommended in the treatment of pulmonary tuberculosis; the method (described by Tranjen) seems to be specially useful in the earlier stages of the disease, and without ill effects even when it is far advanced.

METHOXYCAFFEINE.

$C_8H_9(OCH_3)N_4O_2$.

Nature and Source.—A derivative of the alkaloid caffeine, from the leaves and seeds of coffee, in the leaves of the tea-plant, the seeds of *Paullinia sorbilis*.

Properties and Uses.—White, bulky, crystalline needles, melting at 177° C. The compound has a feebly narcotic action, and is useful in neuralgia and migraine. Subcutaneously injected in 2 per cent. solution, it is credited with anæsthetic properties, superior in certain cases to those of cocaine.

Dose.—4 grains.

MORPHINE SALTS.

$C_{17}H_{17}(HO)_2.NO,\overline{A}$.

Anisate. A white, crystalline powder, soluble in water, less so in alcohol.

Benzoate. A white, neutral powder, soluble pretty freely in hot water (about 1:5). From the hot, saturated solution

the salt crystallizes in hard prisms on cooling. Recommended in the same doses as morphine hydrochloride against asthma.

Borate. This preparation has been suggested for subcutaneous injection, on account of its stability, and for eye-washes, owing to the harmlessness of the boric acid.

The hydrobromide, phtalate and saccharinate, have been described, but are scarcely to be regarded as permanent additions to materia medica.

MUSCARINE.

$C_5H_{15}NO_3$.

Nature and Source.—An alkaloidal principle, obtained from the fungus *Agaricus muscarius.*

Properties and Uses.—A hygroscopic, crystalline substance, readily soluble in alcohol.

Muscarine is a powerful poison, and physiologically an antidote to atropine.

MYRTOL.

Nature and Source.—A fraction of the oil of *Myrtus communis*, boiling between 160° and 180° C.

Properties and Uses.—A clear liquid, of not unpleasant odor, which was recommended (Eichorst), twice a day, as a reliable and prompt remedy against putrid processes of the respiratory tract. According to E. Jahns, myrtol is a mixture of dextro-pinene and eucalyptol, and would be advisedly replaced by the latter.

Dose.—5 minims.

NAPELLINE.

Nature and Source.—An alkaloid, from the root of *Aconitum napellus*, Linné.

Properties and Uses.—An amorphous substance, which, administered subcutaneously, is said to relieve neuralgic pain, and to serve as a substitute for morphine in morphinism.

Dose.—1/6 to 1 grain.

NICOTINE BITARTRATE.

$C_{10}H_{14}N_2(C_4H_6O_6)_2$.

Nature and Source.—A salt of nicotine, the liquid alkaloid ($C_{10}H_{14}N_2$) which is found as malate in the leaves of *Nicotiana tabacum*, Linné.

Properties and Uses.—Fine, white crystals, with a tendency to aggregate; readily soluble in water. The salt is stable, and keeps well even in solution.

This salt is recommended as the most suitable form of administering nicotine in tetanus, strychnine poisoning, etc.

ORMOSINE.

Nature and Source.—An alkaloid, obtained from the seeds of *Ormosia dasycarpa*, a papillionaceous plant of Venezuela.

Properties and Uses.—Small, white crystals, insoluble in water and in dilute alkalies, readily soluble in alcohol and chloroform; m. p. 80° C.

Ormosine resembles opium in its physiological action, but has not been accurately studied.

OSMIC ACID.

$Os\,O_4$.

Nature and Source.—Metallic osmium, as finely divided as possible, is heated to about 400° C., and the volatile tetraoxide caught in cooled receivers.

Properties and Uses.—Lustrous, transparent, yellow needles, with an unbearable penetrating odor (the vapor is poisonous); b. p. about 100° C. Forms a solution with water, which has an intense burning taste.

Osmic acid has been employed subcutaneously in neuralgia, goitre, canceroid and scrofulous ulcers, and internally against epilepsy.

Dose.—$\frac{1}{50}$ grain in pills, subcutaneously employed in the form of 1 per cent solution, which should be always freshly prepared.

OUABAIN.

$C_{30}\ H_{46}\ O_{12}$.

Nature and Source.—A glucoside from the wood of *Acocanthera ouabaio*, an apocynaceous tree of the Somali coast; also obtained from the seeds of *Strophanthus glabrus*, from Gaboon.

Properties and Uses.—White, odorless crystals, with a feebly bitter taste, little soluble in cold, readily in hot water and spirit; insoluble in chloroform, absolute alcohol and anhydrous ether. Melting point 200° C.

Ouabain has been internally used in the whooping cough of children; the attacks diminished in number and intensity.

Dose.—For children, $\frac{1}{1000}$ grain every three hours.

PANCREATIN.

Nature and Source.—One of the digestive enzymes, or a mixture of several, extracted from the pancreatic juice of the pig or calf.

Properties and Uses.—Pancreatin occurs in the form of solid and fluid extracts. It hydrolyses starch, forming sugar, and, in alkaline solution, peptonizes albumen and emulsifies fats. Recommended as a digestive agent *per os*, and as an addition to nutrient enemata, as also for the preparation of peptonized milk, which is often well borne by patients with weak digestion when all other forms of food cannot be retained.

Dose.—From 15 grains to 3 drachms or more, according to the nature of the preparation selected.

PAPAIN.

Nature and Source.—An enzyme from the juice of the unripe fruit of *Carica papaya*, Linné.

Properties and Uses.—An amorphous white powder, very liable to change. Like the animal ferments, it has the power of digesting albuminous substances, with the difference that it is active in acid, alkaline and neutral solutions.

Therapeutically papain is used internally as an aid to digestion, in dyspepsia, gastric and intestinal catarrh, and generally where there is an insufficiency of gastric juice. It is also credited with valuable galactagogue properties, but since it seems to have an abortifacient action its administration requires care. Is further reported to be of service as an anthelmintic. Externally it finds extensive application topically for the removal of the false membranes of croup and diphtheria, and in the treatment of certain indurated diseases of the skin.

Dose.—1½ to 8 grains, in pill, powder, wine or syrup.

PARACOTOIN.

$C_{19}H_{12}O_6$.

Nature and Source.—A principle obtained from the so-called para-coto bark produced by a Bolivian tree, possibly *China coto.*

Properties and Uses.—A bulky, light-yellow, crystalline powder, free from odor and taste, difficultly soluble in water and ether, more readily in alcohol.

This principle, like the closely allied cotoin, has been enthusiastically recommended as anti-diarrhœic. Being anti-putridic and antiseptic, it has a beneficial effect in simple catarrhs of the stomach and intestines, in the diarrhœa of consumptives, and in cholera nostras. Its action has also been praised in the sweats of consumptives.

Dose.—2 to 3 grains in mixture or as powder.

PELLETIERINE.

$C_8H_{15}NO$.

Nature and Source.—An alkaloid from the root-bark of *Punica granatum*, Linné.

Properties and Uses.—A colorless liquid, soluble in 20 parts of water; miscible in all proportions with alcohol, ether and chloroform. It forms crystalline salts with acids, of which the chief are the

Sulphate, a thick liquid substance, and the

Tannate, a yellowish, pulverulent compound, with an astringent taste, soluble in about 700 parts of water and 80 parts of alcohol.

A *hydrobromide* and *hydrochloride* are also prepared.

These combinations have a reputation as anthelmintics.

Dose.—5 to 6 grains, followed in half an hour by a laxative (senna or jalap.)

PEREIRINE.

Nature and Source.—An alkaloid from the bark or root-bark of *Geissospermum laeve* (Pao Pereiro), a member of the order Apocynaceæ.

Properties and Uses.—Has a tonic action, similar to that of gelsemine, but is also antifebrile. Has been used in the form of salts against malarial fever.

Valerianate. A brown, crystalline powder, readily soluble in alcohol, difficultly so in water, insoluble in ether. A *hydrochloride* is also prepared.

Dose.—Up to 30 grains, given some hours before the expected attack.

PHENOXYCAFFEINE.

$C_8H_9(OC_6H_5)N_4O_2$.

Nature and Source.—A derivative of the alkaloid caffeine (*q. v.*).

Properties and Uses.—A white, bulky powder, melting at 142° C.

Therapeutically it is recommended for use in the same way and form as methoxycaffeine (*q. v.*).

PHLORIDZIN.

$C_{21}H_{24}O_{10}$.

Nature and Source.—A glucoside, from the root bark of various trees belonging to the order Rosaceæ.

Properties and Uses.—Long, silky needles, or tufts of needles, sparingly soluble in cold water, but freely taken up by that solvent at 100° C., and by alcohol; m. p. 106° to 108° C., losing water; becomes solid again at 130°, and melts a second time at 170 to 171° C.

Phloridizin produces artificial diabetes in the animals to whom it is given; 8 grains per pound of body weight causes an excretion of sugar, lasting 24 to 30 hours, and amounting to 1½ to 3 drachms. It is employed in physiological research.

PHOTOXYLIN.

Nature and Source.—A nitro-cellulose, prepared from wood-wool.

Properties and Uses.—Soluble in a mixture of equal parts of ether and alcohol, and otherwise very similar to pyroxylin. A 3 to 5 per cent. solution is a thick liquid, which on evaporation leaves a much stronger film than collodium does.

Photoxylin is employed in plastic surgery.

PHYSOSTIGMINE.

$C_{15}H_{21}N_3O_2$.

Nature and Source.—An alkaloid from the seeds of *Physostigma venenosum*, Balfour.

Properties and Uses.—The physical and chemical properties of the alkaloid are well known. More recently two salts have been prepared, and brought under medical notice; both are official in the Pharm. Germ III.

Salicylate. Colorless, or feebly yellow, lustrous crystals, which dissolve slightly in water (1:150), and in alcohol (1:12); the solutions are neutral to litmus. The dry salt is stable, but the aqueous and spirituous solutions soon assume a reddish color.

Sulphate. A white, somewhat hygroscopic, crystalline powder, which dissolves readily in water and alcohol; the solutions are neutral to litmus.

The salicylate is chiefly used in ophthalmology (⅓ to 1:150 of water), but also internally in convulsive affections, in intestinal atony, and as an antidote to atropine.

The sulphate is used in veterinary practice, subcutaneously, against colic.

Dose.—Of the salicylate, internally, $\frac{1}{100}$ to $\frac{1}{60}$ grain; of the sulphate, for horses and cattle, 1½ grain.

PICROPODOPHYLLIN.

Nature and Source.—A neutral principle, from the rhizome of the *Podophyllum peltatum*, Linné.

Properties and Uses.—A crystalline body, regarded as the chief constituent of podophyllin.

Picropodophyllin is credited with laxative and hepatic properties.

PICROTOXIN.

$C_{12}H_{16}O_7Aq.$

Nature and Source.—A bitter principle, obtained from the fruits of *Anamirta cocculus*, Wight and Arnott.

Properties and Uses.—Colorless, lustrous, bitter needles, soluble in alcohol, less so in water and in ether.

Medicinally picrotoxin is used against spinal paralysis, and in the night-sweats of consumptives; externally in skin diseases and as an antiparasitic.

Dose.—$\frac{1}{100}$ to $\frac{1}{10}$ grain. Externally, applied as ointment (3 to 5:250 of fat).

PILOCARPINE.

$C_{11}\ H_{16}\ N_2\ O_2.$

Nature and Source.—An alkaloid isolated from the leaves of *Pilocarpus pennatifolius*, Lemaire, and regarded as belonging to the nicotine group.

Properties and Uses.—The alkaloid itself is a non-crystallizable, soft, viscous mass, very slightly soluble in water, freely so in ether, in alcohol and in chloroform. Chiefly used as

Hydrochloride, which occurs in white microscopic crystals, readily soluble in water and in alcohol, but less so in ether and in chloroform.

Medicinally pilocarpine salts are used externally, by hypodermic injection, as diaphoretics in diseases of the respiratory tract, dropsies, scarlatina, diphtheria, rheumatic affections, certain skin affections, etc. The injections may produce collapse and pulmonary œdema. Regarded as an antidote to ether. Also used to strengthen the hair, in pomades and washes.

Dose.—$\frac{1}{3}$ grain or $\frac{1}{2}$ grain pro die.

PIPERINE.

$C_{17}\ H_{19}\ NO_3$.

Nature and Source.—An alkaloid from the fruits of *Piper nigrum*, Linné.

Properties and Uses.—When pure, piperine is colorless, and has little or no pungency; mostly more or less contaminated with resin, and then yellowish and pungent. Practically insoluble in cold or hot water, or in ether; fairly soluble in alcohol; freely so in sulphuric and acetic acids.

Given internally as a laxative and antipyretic.

Dose.—1 to 10 grains, several times a day, in powder or pills.

PIPERONAL.—(Heliotropin).

$C_8\ H_6\ O_3$.

Nature and Source.—When the alkaloid piperine is boiled with alcoholic potash, potassium piperate crystallizes out in lustrous prisms. By oxidation of piperic acid ($C_{12}\ H_{10}\ O_4$) piperonal is obtained.

Properties and Uses.—Small, white crystals, soluble in alcohol and ether; insoluble in water.

Is antiseptic and antipyritic; but little used on account of its high value. Its chief employment is in perfumery.

Dose.—Up to 15 grains every three hours.

POTASSIUM COMPOUNDS.

Among the long list of combinations which might be classed under this head only two or three require detailed mention.

Auro-cyanide, $KAuCy_4$. White crystals, soluble in water. Subcutaneously injected is rapidly absorbed; does not precipitate albumen.

According to Behring's researches, 1 part of this compound in 25,000 parts of blood serum rendered the latter unsuitable as a medium for the growth of anthrax bacilli. The allied *mercuro-cyanide* (K_2HgCy_4) effects the same in a dilution of 1 : 60,000.

Cantharidate. Used hypodermically by Liebreich in very attenuated solutions in the treatment of tuberculosis (*v.* Cantharidin).

Cobalto-nitrite $K_6Co_2(NO_2)_{12}$, 2 Aq. Yellow microscopic crystals, very little soluble in cold water; insoluble in alcohol and in ether.

Recommended in cases where nitrites are considered indicated, *e. g.* in dyspepsia, cardiac albuminaria, etc. Has been claimed to be more easily regulated in its physiological action than most nitrites.

Dose.—½ grain every two or four hours.

Mercuro-cyanide, *v.* Auro-cyanide.

Osmate. A violet-red crystalline powder, soluble in water. Employed in combination with bromide against epilepsy, and subcutaneously in neuralgias, goitre and neuralgia (*v.* also Osmic acid).

Dose.—$\frac{1}{60}$ grain; $\frac{1}{40}$ grain pro die.

Sozoiodol. (*v.* Sozoiodol).

Tellurate. K_2TeO_4. A white crystalline salt, soluble in water. Has been given in phthisis, with the effect of reducing and even arresting the night sweats. Does not alter the course of the disease. Communicates an intense garlic odor to the breath.

QUASSIIN.

$C_{41}H_{42}O_9$.

Nature and Source.—An indifferent, bitter principle, from the wood of *Picraena excelsa* and of species of *Quassia.*

Properties and Uses.—A crystalline body.

Recommended as a stomachic and tonic for the stimulation of digestion and secretion.

Dose.—$\frac{1}{30}$ to $\frac{1}{3}$ grain.

QUEBRACHINE HYDROCHLORIDE.

$C_{21}H_{26}N_2O_3.HCl$.

Nature and Source.—Salt of an alkaloid from the bark of *Aspidosperma quebracho,* Schlecht.

Properties and Uses.—Internally and subcutaneously in the treatment of dyspnœa.

Dose.—1 to 2 grains.

QUINIDINE TANNATE.

$(C_{20}H_{24}N_2O_2)_2C_{27}H_{22}O_{17}$.

Nature and Source.—An alkaloidal salt, obtained from the bark of *Cinchona pitayensis*, and other species.

Properties and Uses.—An almost tasteless salt. Has been given in dyspepsia, diarrhœa, nephritis and albuminaria. Also recommended in veterinary practice.

Dose.—3 to 12 grains, two to four times daily.

QUININE SALTS.

The number of new quinine combinations is very considerable, but it is very doubtful whether more than one or two of them will obtain a permanent place in materia medica. Following is a full list:

Quinine albuminate.
" ammonio-citrate.
" arsenate.
" borate.
" dihydrobromide.
" dihydrochloride.
" dihydrochl. carbamate
" ethylsulphate.
" ferri-chloride.
" ferri-cyanide.
" ferro-citrate.
" ferro-cyanide.
" ferro-peptonate.
" ferro salicylate.

Quinine glycyrrhizin.
" hydrobromide.
" hydrochl.-citrate.
" hydrofl.-citrate.
" hydrofl.-silicate.
" iodo-hydroiodide.
" lactate.
" oleate.
" peptonate.
" phenylate.
" phenylo-muriate.
" phenylo-sulphate.
" phtalate.
" saccharinate.
" salicylate.

The *ferri-chloride* occurs in dark-brown, lustrous scales, or as a reddish-brown, hygroscopic powder, with a bitter, astringent taste; readily soluble in water and in 70 per cent. alcohol.

It has been recently recommended as an excellent haemostatic, well suited for internal or external use. It may be strewn on bleeding surfaces, snuffed in epistaxis, and applied

in 2 per cent. solution in uterine haemorrhage. Internally has been given in gastro-intestinal bleeding and in hæmoptysis.

Dose.—1½ to 3 grains several times a day in pills, wafers or mixture.

Oleate. A greyish-yellow, granular mass, forming a clear solution in alcohol.

Employed in skin diseases, etc., in the form of ointments, suppositories and the like.

Salicylate. Fine, white needles, difficultly soluble in water, more readily so in alcohol.

This salt combines the properties of quinine and salicylic acid, and hence is considered indicated as an antiseptic and antipyretic in typhus, articular rheumatism, etc.

Dose.—1½ to 8 grains.

QUINOIDINE.

Nature and Source.—A mixture of amorphous alkaloids, obtained as a bye-product in the manufacture of the crystallizable principles of cinchona bark.

Properties and Uses.—A brownish-black mass, insoluble in water, unless the latter be made feebly acid; has a nauseous taste. The two salts named below are also used.

Borate. A cheap quinine substitute (8 to 15 grains pro dosi).

Citrate. A brown, hygrosopic mass, soluble in two parts of hot water, also in alcohol, glycerine and acids.

Dose.—The same as that of quinine.

RETINOL.

Nature and Source.—A product of the destructive distillation of resin.

Properties and Uses.—A yellowish, oily liquid, which boils at temperatures above 280° C.

Retinol is a useful solvent for a large number of the newer remedies, *e. g.*, iodol, aristol, cocaine, as well as of carbolic acid, creasote, phosphorus, and many alkaloids. The solution of phosphorus is very stable, and has been recommended for the external and internal use of the metalloid.

RUBIDIUM AMMONIUM BROMIDE.

$RbBr(NH_4Br)_3$.

Properties and Uses.—A white, crystalline powder, readily soluble in water; its taste is cooling and saline.

This double salt of rubidium was recommended as a substitute for potassium bromide in epilepsy, having the advantage of a more marked sedative action. It has failed, however, to attract attention.

Dose.—1 to 2 drachms daily, in mixture with lemon syrup.

SANGUINARINE NITRATE.

$C_{17}H_{15}NO_4HNO_3$.

Nature and Source.—The salt of an alkaloid, obtained from the root of *Sanguinaria canadensis*.

Properties and Uses.—A stimulant and tonic, in large doses purgative and emetic; also an expectorant.

Dose.—$\frac{1}{12}$ to $\frac{1}{8}$ grain as an expectorant; $\frac{1}{2}$ to 1 grain as an emetic.

SANTONINOXIM.

$C_{15}H_{18}O_2NOH$.

Nature and Source.—A derivation of santonin, obtained by the action on the latter of hydroxylamine hydrochlorate in alcoholic solution under the addition of soda.

Properties and Uses.—White crystals, soluble in alcohol and ether, only difficultly so in water, or in weak alkaline and weak acid solutions; m. p., 162° C.

Santoninoxim is said to be less poisonous than santonin, and is therefore recommended as an anthelmintic; the desired effect is produced without any functional disturbance.

Doses.—For children of 2 to 3 years, 1 grain.
" " " 4 to 6 " 1½ "
" " " 6 to 9 " 2 "
" adults 5 "

divided into two portions, with an interval of 1 to 2 hours, followed by a purgative. Must be repeated for 2 to 3 days, one after the other.

SCILLAIN.

Nature and Source.—A glucoside from the bulb of the squill, *Urginea scilla*, Steinheil.

Properties and Uses.—A colorless or yellowish bulky powder, which forms a red solution in hydrochloric acid.

The compound is diuretic and toxic, resembling the digitalis glucosides.

Dose.—$\frac{1}{60}$ grain, or $\frac{1}{6}$ to $\frac{3}{4}$ grain *pro die.*

SCILLIPICRIN..

Nature and Source.—A principle from the bulb of *Urginea scilla.*

Properties and Uses.—An amorphous, yellowish-white, very hygroscopic powder, readily soluble, and suitable for hypodermic injection.

Scillipicrin is a powerful diuretic, which reduces the activity of the heart.

Dose.—$\frac{1}{60}$ grain.

SCLEROTIC ACID.

$C_{12}H_{19}NO_9$.

Nature and Source.—A principle obtained from the sclerotium of *Claviceps purpurea*, Talasne.

Properties and Uses.—A faintly acid, hygroscopic powder, free from taste and odor; readily soluble in water, difficultly so in alcohol.

Sclerotic acid has been recommended for injection as a substitute for extract of ergot, and also in the treatment of epilepsy. Is inferior to cornutin in gynæcology.

Dose.—½ grain; 5 grains *pro die.*

SCOPARINE.

Nature and Source.—A principle from the tops and twigs of *Cytisus scoparius*, Link.

Properties and Uses.—A feebly acid substance.

Scoparine is diuretic.

Dose.—8 to 15 grains internally, or ½ to 1 grain subcutaneously.

SCOPOLEINE.

Nature and Source.—An alkaloid from the root of *Scopolia japonica.*

Properties and Uses.—In large crystals, little soluble in water; readily soluble in alcohol, ether and chloroform.

In physiological action scopoleine stands between atropine and hyoscyamine, but requires more intimate study.

SILVER POTASSIUM CYANIDE.

$AgK(CN)_2$.

Properties and Uses.—White crystals, soluble in water.

According to Behring this double cyanide has a powerful antiseptic action, while at the same time it is comparatively less poisonous to the organism attacked by the microbes. One part of the compound in 50,000 parts of blood serum formed a medium in which anthrax bacilli could not develop, while the fatal dose of the salt for guinea pigs amounted to $\frac{1}{300000}$ of the body weight.

SODIUM COMPOUNDS.

A number of newer sodium salts have been already described in the preceding section of the work. A few others of more or less importance are described here:—

Chloroborate.—A white, crystalline powder, readily soluble in water.

This preparation is claimed to possess powerful antiseptic properties that may be employed for the preservation of meat, as well as for medicinal purposes.

Gynocardate.—A yellowish-white powder, soluble in water, only partly in alcohol, a turbid mixture being produced.

Silico-fluoride, $Na\ F_2Si\ F_4$.—A white, crystalline powder, only difficultly soluble in water (about ½ per cent.). When moist, it has a strongly irritant action on the skin. Recommended under the name "Salufer" as an antiseptic by W. Thompson. A 2 per mille solution is non-irritant, and can be used for irrigating cavities. It is a powerful disinfectant for gynæcological purposes, and has been also useful as a styptic.

Sulphoricinate. — A brown, syrupy liquid, which readily and completely dissolves in water and alcohol. It forms a good solvent for iodine, iodoform, etc.

Tellurate, Na_2TeO_4.—A white powder, soluble in water.

Like the potassium salt sodium tellurate is an excellent antihydrotic, the night-sweats of phthisis being unfailingly suppressed by it. In common with other tellurium compounds, it communicates a garlic-like odor to the breath, that may be only partially covered by peppermint.

Dose.—1 grain *pro die.*

Tetraborate.—Transparent, glassy masses, which very readily dissolve in cold water (*v.* Boric acid).

SOLANINE.

$C_{42}H_{87}NO_{15}$.

Nature and Source.—An alkaloidal glucoside obtained from parts of various solanaceous plants. Is also present in potato-sprouts.

Properties and Uses.—Acicular crystals, melting at 235° C.; very difficultly soluble in water, more readily so in hot alcohol. Is split up by dilute acids into dextrose and solanidin.

Solanine is not mydriatic. Has been used as an analgesic instead of morphine in neuralgia, the vomiting of pregnancy, in bronchitis, and asthma.

Dose.—1/6 to 1 grain, three times a day, in pill or powder; the hydrochloride has also been used subcutaneously in the same dose.

SPARTEINE.

$C_{15}H_{26}N_2$.

Nature and Source.—An alkaloid obtained, with scoparine, from the tops and twigs of *Cytisus scoparius*, Link.

Properties and Uses.—A volatile oily liquid, very unstable; b. p. 288 C. Only used in the form of salts, of which the most important is the

Sulphate.—Colorless, odorless, transparent crystals, readily soluble in water and alcohol; at 100° C. they lose 21.3 per cent. of water.

Properties similar to those of digitalis have been ascribed to sparteine, but some observers characterize its action as unreliable.

Other salts are the hydrochloride and hydrobromide.

Dose.—Of the sulphate, 1½ to 2 grains, repeated several times a day.

SPERMINE.

C_2H_5N.

Nature and Source.—A base obtained from the seminal fluid of various animals.

Properties and Uses.—A crystalline body, which absorbs water and carbonic acid from the air; readily soluble in water and absolute alcohol, insoluble in ether.

Spermine was specially recommended against nervous and cerebral depression, and has been used in senile and general debility, but further and more intimate study of its properties is still necessary and appears to be going on.

Various salts have been prepared, such as the hydrochloride and phosphate, but not much used.

STRONTIUM COMPOUNDS.

Bromide, $SrBr_2$, 6Aq.—Long, colorless needles, readily soluble in water.

On the recommendation of French medical men, strontium salts have been recently administered in gastric affections, especially in hyperacidity, in Bright's disease, and in epilepsy. Strontium bromide is better borne than other bromine salts, which only too often produce gastric disturbances.

Dose.—30 to 60 grains *pro die*, dissolved in water; in epilepsy this daily quantity can be increased to 6½ drachms.

Lactate, $Sr(C_3H_5O_3)_2$, 3Aq.—A white, granular powder, which forms a clear solution in water.

Recommended in various kidney diseases, associated with albuminaria. Contra-indicated only in renal diseases, with reduced excretion of urine, or where uræmic symptoms appear.

Dose.—Up to 2 drachms daily; ordinarily, however, it may be given in the same doses as the bromide.

STROPHANTHIN.

$C_{16}H_{20}O_8$.

Nature and Source.—A glucoside from the seeds of species of *Strophanthus*.

Properties and Uses.—A white, amorphous, or crystalline, powder, with an extraordinarily bitter taste; freely soluble in water and in alcohol.

Though in some cases inferior to digitalis as a cardiac, it is superior to it in the absence of any disturbing effect upon the respiratory centres. Its action on the vascular system is also less pronounced. The extensive literature of strophanthus contains the records of a very large number of cases in which it has done good service where other cardiacs have failed.

Dose.—$\frac{1}{60}$ to $\frac{1}{30}$ grain in water daily. Rarely hypodermically in doses of $\frac{1}{100}$ grain.

STRYCHNINE SALTS.

$C_{21}H_{22}N_2O_2.\overline{A}$.

The two principal newer combinations of strychnine are with saccharin and arsenium. The

Arseniate is a white, microcrystalline powder, with a bitter taste.

Recommended, especially from America, as a tonic and diuretic, and in the treatment of phthisis.

Dose.—4 to 15 drops of a half per cent. solution (in liquid vaselin) daily.

TANNIN ALBUMINATE.

Properties and Uses.—Is said to be preferable to ordinary powdered or dissolved tannin, in that it has a more agreeable taste and is rapidly absorbed from the stomach, without causing any disturbance. At the same time its astringent action is as marked, or even more so, than that of tannin.

TEREBENE.

$C_{12}H_{16}$.

Nature and Source.—A mixture of several terpenes, obtained by distilling oil of turpentine with sulphuric acid, and subsequently rectifying.

Properties and Uses.—A feebly yellow liquid, with a pleasant aromatic odor reminding of thyme, not very miscible with water, but somewhat more so with alcohol, and freely with ether. Is useful as an aerial disinfectant.

Internally terebene is used as an expectorant and for inhalation in chronic and recurrent bronchitis, and externally for dressing wounds (5 per cent. aqueous solution).

Dose.—4 to 6 or more drops every four hours, in emulsion or tablets.

TERPIN HYDRATE.

$C_{10}H_{18}(OH)_2$, Aq.

Nature and Source.—Prepared by the interaction of a mixture of rectified turpentine oil (4 parts), alcohol (of 80° T) (3 parts), and nitric acid (1 part), in shallow porcelain dishes during some days. A crystalline body separates, which is collected, drained, pressed between bibulous paper, and crystallised in the cold from 95 per cent. alcohol made alkaline with a little potash and soda.

Properties and Uses.—Terpin hydrate occurs in large, colorless and odorless rhombic crystals, with a faint aromatic taste. Soluble in 250 parts of cold (15° C.) or 32 parts of boiling water, in 10 parts of alcohol, 100 of ether, 200 of chloroform, carbon bisulphide and benzene, but less in turpentine. Melting point 116° to 117° C., with separation of the molecule of water.

A primary therapeutical effect of this compound is to increase the secretion of the bronchial mucous membrane; it is therefore indicated in chronic and subacute bronchitis, whooping cough, etc. In larger doses it stimulates renal activity, and hence is given in chronic nephritis. Its value is very probably dependent, to some extent, on its antiseptic properties.

Dose.—As an expectorant 2 to 3 grains, in renal affections 5 to 6 grains, and in whooping cough 20 to 40 grains daily. Can be prescribed in pills, in tablets and in mixture with spirit, syrup and peppermint water.

TERPINOL.

Nature and Source.—The product of boiling terpin, or terpin hydrate, with dilute mineral acids. Is not a simple body but a mixture of terpenes (terpinene, terpinolene and dipentene), with variable proportions of an alcohol, terpineol ($C_{10}H_{17}OH$).

Properties and Uses.—An oily body, with a hyacinthine odor; practically insoluble in water, but readily so in alcohol and ether; sp. gr. 0:852.

Terpineol has been used as a bronchial stimulant.

Dose.—8 to 15 grains in capsules or pills.

Terpineol. The alcohol referred to above is a thick, colorless, optically inactive liquid, with a pleasant hyacinthine odor, and a bitter, feebly pungent taste; s. g. 0.940 (at 15° C.).

It is recommendeded for the deodoration of iodoform.

THEOBROMINE.

$C_7H_8N_4O_2$.

Nature and Source.—An alkaloid obtained from the seeds of *Theobroma cacao*, Linné; a homologue of caffeine, containing a CH_2 group less than the latter.

Properties and Uses.—A white, crystalline powder, sparingly soluble in water, in alcohol and in ether.

Physiologically theobromine closely resembles caffeine, but is said to differ in having no irritating effect upon the nerve centres. Being insoluble it is unsuitable for use, and hence is employed in the form of a double salt (*v.* Diuretin).

THYMOL.

$C_{10}H_{13}HO$.

Nature and Source.—A phenolic stearoptene from the volatile oils of *Thymus vulgaris*, Linné, *Monada Punctata*, Linné, and *Carum ajowan*, Bent. and Hook.

Properties and Uses.—The physical and chemical properties of thymol are well known. Used as an antiseptic for the preservation of anatomical preparations and the embalming of corpses. In association with the well-known automatic door-closing apparatus, is employed as a purifier of the atmosphere, especially in large ocean steamers.

Internally in typhus, rheumatism, gastric fermentation, etc.; also as an antipyretic. Recommended for inhalation in pulmonary gangrene, bronchitis, whooping cough, and for mouth washes, against toothache, etc. In the treatment of wounds a 1 to 10 per mille solution is used; and in skin diseases, ointment and liniments (1 to 5 per cent.).

Dose.—1 to 2 grains in typhus, etc.; 8 to 15 grains as an antipyretic.

TUBERCULIN.

Nature and Source.—A sterilized glycerine extract of pure cultures of the tubercle bacillus, first prepared by Dr. Robert Koch.

Properties and Uses.—A transparent, yellowish liquid, stable in concentrated solution, but liable to change in the dilute condition.

Recommended as a diagnostic agent for the tuberculous diathesis, and as a remedy for the various forms of tuberculosis itself. A 1 per cent. solution is used (or 2 per mille for children) and a special syringe. The greatest care has to be taken in sterilizing the solution, the syringe, etc., and detailed instructions are given with each supply of the remedy. The literature of "Koch's treatment" has attained colossal dimensions, but perhaps definite judgment of its value must be still suspended.

Tuberculocidin is a modification of tuberculin, introduced by Prof. Klebs as free from the sometimes injurious effects of tuberculin, which he ascribes to organic bases. The active substance of "Koch's lymph," according to Klebs, is an albumose, which does not produce the febrile symptoms of the crude substance. Tuberculocidin is put forward as a preparation of this pure albumose.

ULEXINE.

7'. CYTISINE.

VANILLIN.

$C_6H_3OH.OCH_3CHO.$

Nature and Source.—Occurs as a crystalline efflorescence on vanilla pods (*Vanilla planifolia*), also in many beet sugars, and in small quantities in the wood of many plants, where it probably originates in the oxidation of coniferin $\left\{COH-[CH(OH)]_4-CH_2-O-C_6H_3\begin{matrix}OCH_3\\C_3H_4(OH)\end{matrix}\right\}$.

Properties and Uses.—Acicular crystals, melting at 80° C., b. p. 285°C., subliming unchanged. Soluble in alcohol, ether and chloroform; less readily in water. Smells and tastes like vanilla.

Has been recommended as a stimulant in atonic dyspepsia.

VIEIRIN.

Nature and Source.—A bitter principle, from the bark of *Remijia vellozii*, a Rubiaceous plant, found in Brazil.

Properties and Uses.—An amorphous, white substance, with an aromatic odor and bitter taste; m. p. 120° C. It is readily soluble in alcohol and in chloroform.

Esteemed in Brazil as a substitute for quinine in the treatment of fevers, and as a general tonic.

Dose.—1½ to 3 grams several times a day.

WRIGHTINE.

$C_{24}H_{40}N_2.$

Nature and Source.—An alkaloid from the barks of *Wrightia antidysenterica* and *Holarrhena antidysenterica*.

Properties and Uses.—Said to possess the properties of the drugs from which it is isolated, and hence recommended in drarrhœa and dysentery. Possibly it is also febrifuge and anthelmintic.

ZINC COMPOUNDS.

Chrysophanate. A brownish-red powder, that is readily taken up by water (made alkaline), and consequently is dissolved by the alkaline secretions of wounds.

Gynocardate. A yellowish, granular powder, insoluble in water and diluted acids, readily soluble in ether, in alcohol and chloroform.

Recommended in the treatment of those forms of skin disease in which gynocardic acid has been used.

Permanganate. In crystals, very similar to those of the potassium salt; very hygroscopic and readily soluble in water.

Used in the treatment of urethritis of all kinds; is non-irritant in dilute solutions (1:4000). Alcohol, vegetable extracts and the like, must not be ordered with it, as explosive mixtures are formed.

Sulphydrate. $Zn(SH)_2$. A white precipitate, that must be kept under water, as it readily decomposes on keeping.

Used internally and externally with success in the treatment of chronic eczema, psoriasis and vegetoparasitic dermatoses. The ointment adopted was of the strength 10 per cent., with lanolin and lard (2:3).

Dose.—½ to 2 grains, several times a day, made up into pills with extract of gentian.

TABLES

OF

DOSES, SOLUBILITY, MELTING and BOILING POINTS of NEW REMEDIES.

Prof. Demme, of the Jenner Children's Hospital, Berne, gives the following:—

Dosage of Antipyretics for Children.

	Children of		
	2—4 years.	5—10 years.	11—15 years.
Acetanilide, 1–3 times daily, pro dosi.....	1—1½ grains	2— 4 grains	4— 5 grains
Antipyrine, 2—3 times daily, pro dosi.....	3—6 grains	8—10 grains	12—15 grains
Phenacetine, single dose....	2—4 grains	4— 5 grains	8 grains
Quinine salts, single dose ...	3—6 grains	8—10 grains	10—15 grains
Salol, 3—4 times daily, pro dosi	4—6 grains	8—12 grains	12—15 grains
Thallinesulphate every 2 hours	⅙ grain	⅓ grain	½— 1 grain

TABLE I.

Average Doses of New Remedies.

	Pro dosi.	Pro die.
Acetanilide	3— 8 grains	45 grains
Amylene hydrate	45—60 "	2 drms.
Antipyrine	15—30 "	
Benzanilide	15—45 "	
Benzosol	4—12 "	12—36 grains
Betol	5— 8 "	15—30 "
Bromacetanilide	2— 8 "	
Bromoform	1— 2 minims	5—20 minims
Bromol	1 grain	8 grains
Chinoline salts	5—20 grains	
Chloralamide	30—45 "	1½ drms.
Chloralammonium	30—45 "	1½ "
Chloralurethane	10—40 "	
Creasote	3 minims	
Creolin	5 "	
Dithiosalicylic acid II.	8 grains	30 grains
Diuretin	15 "	45—90 "
Ethyl bromide	5—10 drops	
Euphorin	6— 8 grains	20—30 grains
Exalgine	½— 4 "	
Guaiacol	2 minims	15 minims
Guaiacol carbonate	6— 8 grains	1½ drms.
Hydracetine	⅙— 1 grain	2 grains
Hydroquinone	3— 8 grains	
Hypnal	15—30 "	
Hypnone	3— 8 minims	
Ichthyol	4—20 "	
Iodol	3 grains	8—15 grains
Iodopyrine	8—24 "	
Methacetine	5—15 "	
Methylal	15—30 minims	2 drms.
Methylene blue	1½— 8 grains	
Naphtalene	1— 2 "	8 grains

TABLE I.—*(Continued.)*

	Pro dosi.	Pro die.
Orexine hydrochloride	5— 8 grains	
Paraldehyde	½— 1 drm.	
Pental (by inhalation)	2— 3 drms.	
Phenacetine	8—12 grains	1½ drms.
Phenocoll hydrochloride	8—15 "	1½ "
Piperazine	15 "	45 grains
Resorcin	3— 8 "	45 "
Salicylamide	3— 5 "	15 "
Salipyrin	15 "	
Salol	15—30 "	2 drms.
Sodio-theobromine salicyl. (*v.* Diuretin)		
Sodium ichthyolsulphonate	3 grains	10 grains
" paracresotate	15—30 "	
Somnal	30 minims	
Sulphonal	15—30 grains	1½ drms.
Tetronal	15—30 "	1½ "
Thalline salts	2— 5 "	
Thiol (liquid)	4—20 minims	
Thymacetin	5—15 grains	
Tribromophenol (*v.* Bromol)		
Trional	15—30 grains	1½ drms.
Urethane	15—40 "	

TABLE II.

Solubility of New Remedies

in Water and Spirit.

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Acetanilide.....	200	10	In about 18 of boiling water or 40 of glycerine. Ph. G. 194 pts. of water and 3½ of alcohol.
Amylene hydrate ...	8	freely sol.	Saturated aqueous solutions become turbid when warmed.
Anthrarobin.....	insoluble	5	Dissolves in aqueous alkalies, also in glycerine.
Antipyrine	1	1	
— benzoate..	slight. sol.	freely sol.	Also taken up by ether.
Apyonin	little sol.	freely sol.	
Aristol.....	insoluble	slight. sol.	Taken up by trituration with fatty oils.
Benzanilide.....	insoluble	60	
Benzonaphtol	insoluble	soluble	
Benzophenoneid	100		
Benzosol.....	insoluble	soluble	Readily soluble in hot alcohol.
Betol	insoluble	diffic. sol.	In about 3 of boiling alcohol.
Bromacetanilid	insoluble	diffic. sol.	
Bromoform	300	freely sol.	
Bromol	prac. insol	freely sol.	Also soluble in ether, chloroform, glycerine and oils.
Chinoline	prac. insol	5	
— salicylate ..	80	freely sol.	
— tartrate	80	150	

TABLE II.—*(Continued.)*

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Chloralamide.....	10	2—3	Is only slowly taken up by water; must not be heated.
Chloralammonium ..			Chloralammonium decomposes even in the cold.
Chloral-urethane....	insoluble	soluble	Decomposes when heated in solution like all these chloral compounds.
Creolin		soluble	Forms emulsion with water.
Creasote	prac. insol	freely sol.	Dissolves in 120 pts. of hot water.
Cresalols.....	insoluble	readily sol	Also taken up by oils.
Cresol iodide.....	insoluble	readily sol	Taken up by fatty oils.
Cresotic acids	diffic. sol.	readily sol	
Dermatol	insoluble	insoluble	
Di-iodo-β-naphtol....	insoluble	sparingly	Abundantly taken up by chloroform.
Dithiosalicylic acid I	insoluble	insoluble	
" " II	insoluble	readily sol	
Diuretin	freely sol.		
Ethyl bromide.....	insoluble	soluble	Also miscible with ether, chloroform and oils.
Ethylene bromide ..	insoluble	fr'ly misc.	
Euphorin	insoluble	readily sol	Taken up by mixtures of alcohol and water (wines).
Europhen.....	insoluble	readily sol	Also taken up by fatty oils.
Exalgine.....	diffic. sol.	readily sol	

TABLE II.—*(Continued.)*

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Fluorescein	soluble		
Gallacetophenone...	about 500	readily sol	Readily soluble in hot water and a 4 per cent. solution may be made in 30 per cent. sod. acetate.
Guaiacol	85	readily sol	
Hydracetine.....	50	readily sol	Taken up by 8–10 boiling water.
Hydronaphtol	little sol.	soluble	
Hydroquinone.....	diffic. sol.	readily sol	Also readily in hot water.
Hydroxylamine hydr.	1	15	Also in glycerine.
Hypnal.....	5—6		
Hypnone	insoluble	readily sol	Also miscible with fatty oils.
Ichthyol	freely sol.	partly sol.	
Iodantipyrine	diffic. sol.	diffic. sol.	More freely soluble in the hot menstrua.
Iodol.....	prac. insol	3	Alcohol solutions are precipitated by water, but not by glycerine.
Iodophenine		soluble	Evolves iodine when merely mixed with water.
Kairin	6	20	
Lanolin.....	insoluble	80 (78°C.)	Readily miscible with an equal weight of water.
Lysol.....	freely sol.	freely sol.	
Mercury sozoiodol ..	500		More soluble in solution of common salt.

TABLE II.—*(Continued.)*

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Metaldehyde	insoluble	readily sol	
Methacetine	530	readily sol	Also taken up by glycerine.
Methylal	3	readily sol	Miscible with oils.
Methyl chloride.....			Water absorbs 4 and alcohol 35 volumes.
Methylene-blue.....	slight. sol.	readily sol	
— chloride .	slight. sol.	readily sol	
Microcidin	3		
Naphtalene.....	insoluble	diffic. sol.	Readily soluble in hot alcohol; also taken up by fatty and essential oils.
Naphtol.....	1000	readily	Solubility in water is increased by the presence of boric acid.
Orexine hydrochl....	freely sol.	freely sol.	
α-Oxynaphtoic acid .	prac. insol	10	Somewhat soluble in hot water.
Paraldehyde	10	readily sol	A solution saturated at 15° separates paraldehyde when heated. Ph. G. 8½ pts. of water.
Pental	insoluble	freely sol.	
Phenacetine	prac. insol	diffic. sol.	Ph. G. 1,400 pts. of water and 16 pts. of alcohol.
Phenocoll acetate...	3½		
— carbonate.	insoluble		Readily dissolved by weak acids.
— hydrochl .	16		
— salicyl ...	soluble		

TABLE II.—*(Continued.)*

	1 part dissolved in		Remarks.
	Water (15°)	Spirit (15°)	
Piperazine	very sol.		
Potass. sozoiodol ...	50		
Pyoctanin, blue ... (Methyl-violet)	50 (?)		Generally used in 1 per cent. solutions and upwards.
Pyridine		1	Miscible with water in all proportions.
Pyrocatechin	soluble	soluble	
Resopyrin	insoluble	5	
Resorcin.....	2	readily sol	Ph. G. 1 in 1 of water and 2 in 1 of alcohol.
Saccharin	400	30	
Salicylamide	250	soluble	
Salipyrin.....	diffic. sol.	readily sol	
Salol	insoluble	10	Alcoholic solutions form emulsions with water.
Salophen	insoluble	freely sol.	
Sodium paracresot ..			Soluble in about 24 parts of warm water.
— sozoiodol...	14		
Sozoiodol	readily sol	readily sol	Also taken up by glycerine.
Sulphaminol	insoluble	soluble	
Sulphonal.....	450	65	B. B. Add.: "in about 50 fl. parts of cold rectified spirit."
Sulphosalicylic acid .	readily sol	readily sol	
Tetronal	450	readily sol	
Thalline sulphate ...	7	100	2:10 of boiling water.
— tartrate....	10	slight. sol.	
Thiol.....	soluble	soluble	

TABLE II.—*(Continued.)*

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Thiophen	insoluble		
Thioresorcin		diffic. sol.	
Thymacetin	diffic. sol.		
Trional	320	readily sol	
Urethane	1	0.6	
Zinc sozoiodol.....	20	soluble	

TABLE III.

Melting and boiling points of New Remedies,

in Centigrade degrees.

	M. p.	B. p.	S. g. & Remarks
Acetanilide.....	114°	295°	B. P. Add: m. p. = 112.8° C.
Amylene hydrate ..	—12°	102.5°	S. g. 0.81
Antipyrine	113°		B. P. Add: m. p. = 110° C.
Benzanilide.....	163°		
Benzonaphtol	110°		
Benzosol.....	50°		
Betol	95°		
Bromacetanilide ...	165°		
Bromoform.....	4.5°	149°–150°	S. g. 2.9
Bromol	95°		
Chinoline		237°	S. g. 1.084
Chloralamide.....	115°		
Chloral-ammonium.	62°– 64°		
— -urethane...	100°–103°		
Cresalol, ortho-....	35°		
— meta-	74°		
— para-	39°		

TABLE III.—(*Continued.*)

	M. p.	B. p.	S. g. & Remarks
Cresol, ortho-	31°	188°	
— meta-		201°	
— para-	36°	198°	
Cresotic acid, ortho-	160°		
— — meta-	177°		
— — para-	151°		
Ethyl bromide		38°– 39°	S.g. 1.38—1.39
— chloride		10°	Very inflamm-
Ethylene bromide..		191°	S.g. 2.163 [able
Euphorin	51°		
Europhen	110°		"Sinters" at 70°
Exalgine	100°	240°–250°	
Guaiacol		200°–202°	S. g. 1.117
— carbonate ...	148°–150°		
Hydracetine	128°–129°		
Hydroquinone	172.5°		When rapidly heated it decomposes
Hypnal	67°– 68°		
Hypnone	20.5°	210°	S. g. 1.032
Iodantipyrine	160°		
Iodophenine	130°–131°		
Iodol			Decomposes between 140° and 150°
Lanolin	40°– 44°		B. P. Add: 37°.8 and 44°.4
Metaldehyde			Sublimes without melting at 112°—115°, being partly decomposed.
Methacetine	127°		Distils unchanged.
Methylal		42°	S. g. 0.855
Methyl chloride....		21°	S. g. 0.9915 (at –23.7° C.)

TABLE III.—(*Continued.*)

	M. p.	B. p.	S. g. & Remarks
Methylene chloride.		41°– 42°	S. g. 1.354
Naphtalene.....	80°	218°	
Naphtol.....	123°	286°	
α-Oxynaphtoic acid	185°		Decomposes as it melts.
Paraldehyde.....	10°	124°	S. g. 0.998
Pental.....		38°	Is highly inflammable.
Phenacetine.....	135°		
Phenocoll.....	115°		
Piperazine.....	104°	145°	
Pyridine.....		117°	S. g. 0.9858(0°C)
Pyrocatechin.....	104°	240°–245°	
Resopyrin.....			"Melts very readily"
Resorcin.....	118°	276°	Ph. G.: melts at 100°–111°
Saccharin.....	200°		Decomposes readily when heated.
Salicylamide.....	142°		
Salipyrin.....	91.5°		
Salol.....	42°– 43°		
Salophen.....	187°–188°		
Sulphaldehyde	—2°		
Sulphaminol.....	155°		
Sulphonal.....	125°–126°		B. P. Add. 125°.5
Tetronal.....	85°		
Thalline sulphate..	100°+		Decomposes above the m. p.
Thiophen.....		84°	
Trional.....	76°		
Urethane.....	47°– 50°	170°–180°	Scarcely decomposes even when boiled.

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